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COMMUNICATIONS

THIRD NERVE REGENERATION*†

A CLINICAL EVALUATION

BY

FRANK B. WALSH

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My first and most pleasant duty is to thank the members of the Irish Ophthalmological Society for inviting me to deliver the Montgomery Lecture for 1957 at this joint meeting with the Society of British Neurological Surgeons. It is an honour that I appreciate deeply and shall always consider as a highlight in my professional life.

The selection of a topic has given me much concern. I am deeply disappointed that I am unable to present something new, but new information is hard to come by. All that I am about to say has been said before; possibly it has not received quite the attention it merits from those of us who, as clinicians, try to utilize basic investigations. My interest in regeneration of the third nerve as an explanation for abnormal eyelid and eyeball movements was stimulated by studies made with Doctor Walter Dandy on saccular aneurysms. This paper deals with acquired third nerve paralysis, and brief mention is made of differential diagnosis.

Regeneration of Nerves

Only a few facts regarding nerve regeneration are mentioned here as an introduction to the particular features of third nerve regeneration with which this paper is concerned.

It is established that motor and sensory nerves regenerate; also it seems reasonably certain that autonomic nerves regenerate. Undoubtedly regeneration occurs in peripheral nerves, but it is doubtful that it occurs when interruption has been central.

When a nerve has been severed or crushed, there is degeneration of the axons in the severed fragment. If and when regeneration occurs, there are likely to be more axons in the regenerated nerve than were present before the nerve was interrupted. Axons develop from the cut end of the nerve which has been severed and from collateral nerves which have not been severely damaged (Nageotte, 1932). There is free sprouting of new fibres from the central stump, and cords of Schwann cells form in the peripheral

* The Montgomery Lecture, delivered at Trinity College, Dublin, on May 17, 1957, on the occasion of a joint meeting of the Irish Ophthalmological Society and the Society of British Neurological Surgeons.

† Received for publication May 30, 1957.

segment of the nerve, so that the new fibres are conducted to the end organ (Young, 1942). The newly-formed neurons reach the empty tubes (Schwann's tubes) which before the degeneration contained functioning neurons (Gutmann and Young, 1944; Edds, 1953). In the distal end of the severed nerve there is a tendency toward endoneural tube shrinkage (Sunderland and Bradley, 1950). Regenerating axons have the capacity to bridge long gaps in damaged nerves as has been shown by Sunderland (1953), who supported the idea that the distal stump influences the growth and position of the regenerating axons. There is some evidence that chemical agents released by the denervated muscle, at least in the instance of motor nerves, may play a part in the regeneration phenomenon (Edds, 1953).

Ford and Woodhall (1938) studied regeneration in cranial, spinal, and autonomic nerves. Their findings as regards the facial and oculomotor nerves are described subsequently in this paper. They described the "crocodile tear" and auriculotemporal syndromes as dependent upon the misdirection of regenerated fibres. Regeneration of the medial and ulnar nerves resulted in misdirection and mass action as well as sensory changes which are not considered here. An odd example of misdirection was described by Robinson (1951), who found, in individuals who had suffered a brachial plexus injury at birth, that there were movements in the paralysed limb associated with deep inspiration. These movements varied according to the nature of the brachial plexus palsy.

As regards the newly-formed axons in the regenerated nerve, Ford and Woodhall (1938) cited an experiment of Ramon y Cajal (1928). He severed the sciatic nerve of a cat where it was composed of two separate nerve trunks, the peroneal and the tibial. The regenerating fibres of the tibial nerve entered the distal stump of both the tibial and the peroneal nerve, and those arising in the proximal stump of the peroneal nerve entered both distal stumps in the same way.

Cajal stated:

> "Those sprouts which reach the peripheral stump enter it in great disorder; some sheatth have no sprouts and the great majority, if not all, of the sheaths, instead of receiving the outgrowth of the same axon which was present in them before the operation, are invaded by sprouts which have come from axons in other regions of the central stump. Thus, the observed facts compel us to reject the supposition of those authors who believe that the newly-formed fibre infallibly ends in the old sheath of the peripheral stump and unerringly restores the old terminal arborization, thus preserving the anatomical and physiological individuality of the pre-existing conductor. On the contrary the errors and incongruences are so many that one wonders whether the whole mass of sprouts which penetrate into the peripheral stump is not entirely superfluous, seeing that the connections between central neurons and the peripheral structures which formed, since the embryonic period, such as intimate anatomical and dynamic whole, are now so disturbed and confused. Moreover, in cases of rapid nervous reunion after hemisection or complete sections with small scar, sensibility and movement are only more or less imperfectly restored." (Ford and Woodhall, 1938.)

Aetiology and Occurrence of Third Nerve Paralysis

Acquired paralysis of the third nerve, according to my experience, originates in the following order of frequency:

(1) aneurysms;
(2) trauma;
(3) tumour;
(4) diabetes;
(5) inflammation;
(6) ophthalmoplegic migraine.

(1) Aneurysms have accounted for more examples of regeneration of the third nerve in my practice than has any other aetiological factor. From the statistical point of view this is of no importance because it would vary widely in different centres.

(2) Trauma is a frequent cause of third nerve paralysis. Practitioners who are engaged in an industrial practice often see such cases. Turner found third and sixth nerve paralysis to occur about equally often as a result of war trauma.

(3) Tumour is a frequent cause of third nerve paralysis. Usually in such cases the paralytic involvement is not an isolated one. In my experience regeneration of the third nerve with misdirection of fibres is rarely present as a result of tumour.

(4) and (5) Diabetes and inflammation are infrequent causes of third nerve paralysis. I have seen these aetiologies about equally often. I have not had experience with total third nerve paralysis with herpes zoster; seemingly, incomplete involvement is the rule.

(6) Ophthalmoplegic migraine is quite a rare affection. In the few cases I have encountered third nerve paralysis has been present.

Progress of Third Nerve Paralysis.—Any of several developments may characterize third nerve paralysis:

(1) There may be complete recovery. Presumably either no or only slight degeneration has occurred.
(2) The paralysis may persist unchanged.
(3) Only a change in the pupil may remain as evidence of the paralysis.
(4) There may be incomplete recovery as regards the ophthalmoplegia.
(5) There may be recovery with evidence of misdirection of the regenerated fibres, and in such cases there may be pupillary changes which are characteristic.

The situation as regards the pupil in cases of third nerve paralysis is briefly stated:

(*a*) There may be a return of the pupil to normal;
(*b*) The pupil may remain widely dilated and fixed to light stimulation, both direct and consensual;
(*c*) It may become smaller than its normal fellow of the opposite side, and it may remain sluggish to light stimulation;
(*d*) The pupil may become of Argyll Robertson type when it shows evidence of misdirection of regenerated fibres (Ford, Walsh, and King, 1941).

Phenomenon of Misdirection of Regenerating Fibres.—I have used this title as being possibly more informative than "aberrant regeneration", but in fact the terms are synonymous. Although we are here concerned with the phenomenon as it is observed after third nerve paralysis, brief mention is now made of regeneration of the seventh nerve because such

regeneration received much study long before the phenomenon as it affects the third nerve received any considerable attention. It would be expected that the pattern of regeneration of these two nerves might be similar, because both nerves supply several muscles. It might be anticipated that regeneration of the seventh nerve could be responsible for changes in glandular function, and this is seen in the instance of "crocodile tears". Since the third nerve innervates the pupil, it would seem likely that pupillary anomalies could develop on the basis of regeneration, as does in fact occur.

In the case of the seventh nerve partial recovery from paralysis occurs in many instances within several months after the nerve has been paralysed. Such recovery is characterized by the development of associated movements which occur in varying degree, yet have a fairly constant pattern. When an effort is made to approximate the eyelids on the affected side, there is an associated contraction of muscles at the corner of the mouth and of the homolateral side of the chin. When an individual with facial paralysis whose facial nerve has regenerated attempts to bare the teeth, the eyelids close on the homolateral side (Fig. 1).

FIG. 1.—Regeneration of right facial nerve.
(A) Increased tone in the right facial muscles.
(B) An attempt to bare the teeth results in closing the right eye.

Lipschitz (1906) suggested that these associated movements, which are involuntary, were due to the misdirection of regenerating fibres. He acknowledged that the concept had already been mentioned by Lamy (1905). Ramon y Cajal (1928) supported the idea, and for a time it was accepted by Wartenberg (1946), but he later rejected the idea of misdirected (or aberrant) fibres in the regeneration of both the seventh and the third nerves. It may also be remarked that, when seventh nerve paralysis develops later after injury or when it clears early (that is, within a matter of 2 or 3 weeks), there usually is no remaining evidence of paralysis.

REGENERATION OF THIRD NERVE.—The third nerve normally supplies the levator muscle of the upper eyelid, the medial, superior, and inferior rectus muscles, and the inferior oblique muscle. In addition, it supplies the sphincter of the pupil. The superior branch of the nerve supplies the levator and the superior rectus muscles; the inferior branch supplies all other muscles supplied by the third nerve, including the pupil. The fibres which proceed to the pupil are ultimately carried in the branch to the inferior oblique muscle. The upper eyelid is elevated through the contraction of the levator muscle. When elevation of the lid occurs, there is a synchronous relaxation of the orbicularis muscle (innervated by the seventh nerve). The upper eyelid is lowered when the eye is closed by contraction of fibres of the orbicularis, and there is synchronous relaxation of the levator. The mechanism of this downward movement of the upper eyelid (following movement) when the eye is lowered is not fully understood, but it is of interest that it occurs in the presence of a facial nerve paralysis. In part, the following movement is due to gravity. In part it is due to relaxation of the levator. The close association (osmotic attraction) between the eyelid and the eyeball may explain part of the following movement. The eye is adducted principally by the medial rectus muscle but in addition the superior and inferior rectus muscles have slight adducting power. When the medial rectus muscle is contracted, there is relaxation of the lateral rectus muscle. Conversely, when the lateral rectus is utilized there is relaxation of the medial rectus. All this is in conformity with the theory of reciprocal innervation of the ocular muscles (Sherrington, 1894): if one ocular muscle is contracted its opponent is relaxed.

During regeneration of a damaged third nerve, axons which were originally destined for the levator may in some instances reach that muscle, but other such axons may reach the medial or inferior rectus or the inferior oblique muscles, axons destined for the superior rectus may reach the inferior rectus, and so on. Thus it would seem that with the third nerve, as with the seventh, a mass contraction might develop, and this does in fact happen.

In a classical case of regeneration of the third nerve characterized by misdirection of regenerated fibres, the upper eyelid is elevated when the eyeball is adducted, voluntarily or involuntarily. It is this elevation of the upper eyelid which is so frequently described as the pseudo-Graefe phenomenon. When an effort is made to look up or down with the affected eye, the attempted movement is not obtained because contraction of the superior rectus, occurring at the same time as contraction of the inferior rectus (as well as of other muscles innervated by the third nerve) or *vice versa*, makes vertical movement of the eye impossible. In these circumstances the eye turns in, and the upper eyelid becomes elevated or remains so (Fig. 2, overleaf).

On the basis of reciprocal innervation, as enunciated by Sherrington and as illustrated above, when the affected eye is *abducted* the upper eyelid would be lowered and the outward movement of the eye would be of full range.

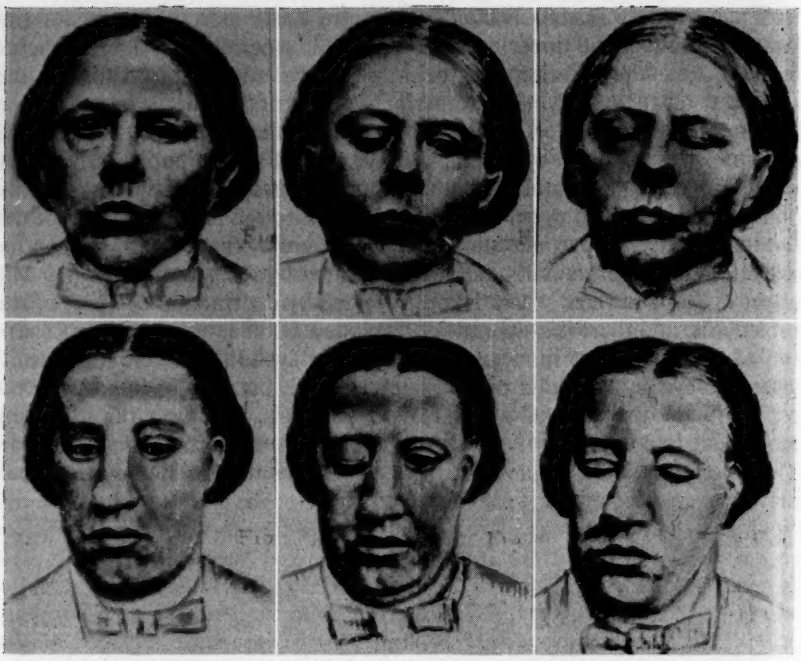

FIG. 2.—Left third nerve palsy. With the eyes in the primary position they appear normal. When an effort is made to adduct the right eye or to direct the gaze downward, the left upper eyelid is raised and the left eye fails to move down (Gowers, 1879).

Associated with the abnormalities of ocular movement just described, a type of Argyll Robertson pupil may develop as part of the misdirection syndrome. The ultimate features of the pupil after third nerve paralysis have already been stated. With the phenomenon now under consideration, the pupil, which may be large or small, fails to react to direct light. It becomes narrowed when the eye is adducted, whether fixation is on a near object (convergence) or on a distant object. Presumably the iris sphincter receives not only pupillary fibres but also others originally destined for the medial rectus or other muscles supplied by the third nerve.

When a "mass movement" occurs in fully-developed cases with misdirection a low-grade enophthalmos is developed. This is explained on the basis of the retracting influences of the contracted recti muscles. This feature has not been described previously so far as I am aware. I hesitate somewhat to mention it since I have been unable to measure the enophthalmos satisfactorily in any case, but Dr. Frank R. Ford is convinced, with me, that it is part of the fully-developed syndrome.

The misdirection phenomenon does not always occur in classical form as has been described above, since presumably, to obtain "full" misdirection,

the third nerve paralysis would have to be complete; but fragmentary examples of the phenomenon are often observed.

SOME EARLY STUDIES OF THIRD NERVE REGENERATION.—The earliest contributions were made in the 1890s. It was at this time that the unfortunate eponym, "pseudo-Graefe sign", was given to the phenomenon of upper-lid retraction. As Wartenberg (1946) noted, after nerve regeneration the upper eyelid does not only "lag" (wherein the title would be reasonable) when an effort is made to lower the eyeball on the affected side, but (particularly when adduction is also attempted) it becomes sharply elevated. Such a movement is obviously an associated movement; it is involuntary and cannot be suppressed. Gowers (1879), in describing several ocular movements, pictured partial recovery from third nerve paralysis as characterized by retraction of the upper eyelid (Fig. 2). Fuchs (1893, 1917) also described the phenomenon, accepting the hypothesis of aberrant regeneration as has been outlined above. He thought that there was retrograde degeneration and that the phenomenon was associated with nuclear involvement. The abnormal behaviour of the upper lid has since often been referred to as Fuchs's sign. Wilbrand and Saenger (1900) showed retraction of the upper eyelid in an individual who exhibited a total third nerve paralysis; the abnormal behaviour of the upper eyelid was attributed to the action of the frontalis. Bielschowsky (1935) remarked upon retraction of the upper eyelid as occurring in some cases of third nerve paralysis, and stated that this was an evidence of regeneration and entirely different from what he had described as cyclic oculomotor paralysis in which there is recurrent elevation of the upper eyelid on the affected side. He suggested that most cases of misdirection originated as the result of injury at the base. He pointed to the similarity between the retraction of the lid in these cases and the paradoxical elevation of the upper eyelid which occurs in congenital cases of jaw-winking (Marcus Gunn phenomenon). He described five cases (three of fracture, one of syphilis, and one with aetiology not determined) and produced four series of photographs. In all instances pronounced elevation of the upper eyelid occurred when the affected eye was adducted, and the elevation was greatest when, at the same time, an effort was made to look down.

Bender and Alpert (1937) and Bender and Fulton (1939) have made valuable contributions. Bender (1954) subscribed to the idea of faulty regeneration of the third nerve; in this communication he suggested the dual innervation of the orbicularis (third and seventh nerves). Bender and Fulton (1939) described experimental section of the third nerve in monkeys. Regeneration was characterized by ophthalmoplegia and lid retraction as has already been outlined. Inability to look up or down resulted from simultaneous contraction of the superior and inferior rectus muscles. By sectioning the superior rectus muscle, an experimental animal could move

the eye downward; by sectioning the inferior rectus, the eye could be moved upward. They also observed the Argyll Robertson pupil in their experimental animals.

I have mentioned regeneration of the third and seventh nerves according to the hypothesis of Lipschitz (1906) as affecting only peripheral nerves. What may be considered as an alternative concept was described by Wartenberg (1946), who criticized the idea of peripheral misdirection of regenerating fibres and attempted to show that the associated movements described above represent the influence of a central lesion which has resulted from a retrograde degeneration. Years earlier Fuchs (1917) had suggested that a central lesion was responsible, and that it served to spread impulses from the cerebrum to various part of the third nerve nucleus.

A third possible mechanism accounting for the characteristic associated movements was mentioned by Bender (1954) in commenting upon a bilateral case of aberrant regeneration of the third nerve, which was presented and described by Norton and Wetzig (1954). The hypothesis is that the denervated muscle has become sensitized to some agent, chemical, mechanical, or electrical.

Levin (1952) made a contribution of prime importance; he produced histopathological evidence that seems to establish the concept of peripheral misdirection. He remarked that anatomical studies on the third nerve after regeneration had been made only by Köppen (1894), who had studied a case characterized by lid retraction and found changes in the peri-aqueductal grey matter, but no changes in the nerve cells, tracts, or nerve roots. Levin's patient, an elderly woman, was shown at autopsy to have had an aneurysm arising from the left internal carotid artery at its junction with the posterior communicating artery. This aneurysm had caused haemorrhages on several occasions, and death ultimately occurred. Anomalous eye movements had been observed on the side of the aneurysm with elevation of the upper eyelid when adduction was attempted. Adduction was not fully performed. Upward and downward movements of the eye were somewhat diminished in amplitude. There was mild ptosis on abduction of the eye. There were no pupillary changes suggesting an Argyll Robertson pupil. Levin remarked upon the third nerve paralysis never having been complete, and that lid retraction in such a case was remarkable. He felt that probably only a few third nerve fibres were affected at any time so that there was never great loss of function. At the autopsy neuromatous changes were found in the roots of the oculomotor nerve (Figs 3 and 4, opposite). Cells were collected in interlacing fascicles with palisaded nuclei; each cell was surrounded by an endoneural sheath. In cross-section views axis cylinders were seen penetrating the tissue.

ELECTROMYOGRAPHY AND NERVE REGENERATION.—Recently electromyography has been used in the study of the extra-ocular muscles. The potentials

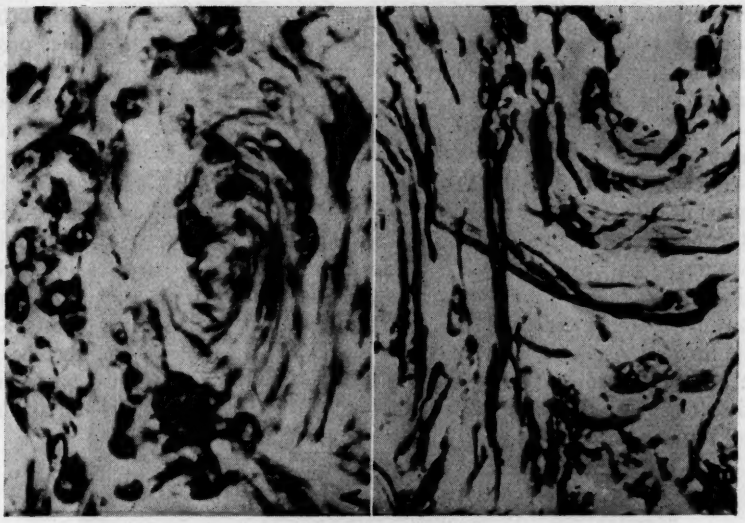

FIG. 3 (From Levin, 1952).

(A) Spiral formation of neurites and cells arranged about a minute hollow tube. Above is a portion of retiform tissue (fasciculated tissue in cross-section) composed of tubes, fibres, and nuclei. Bodian preparation, counterstained with Masson's trichrome stain.

(B) Elongated cells (tubes) incorporating nerve fibres. Note varicosities on fibres. Bodian; ×1,000.

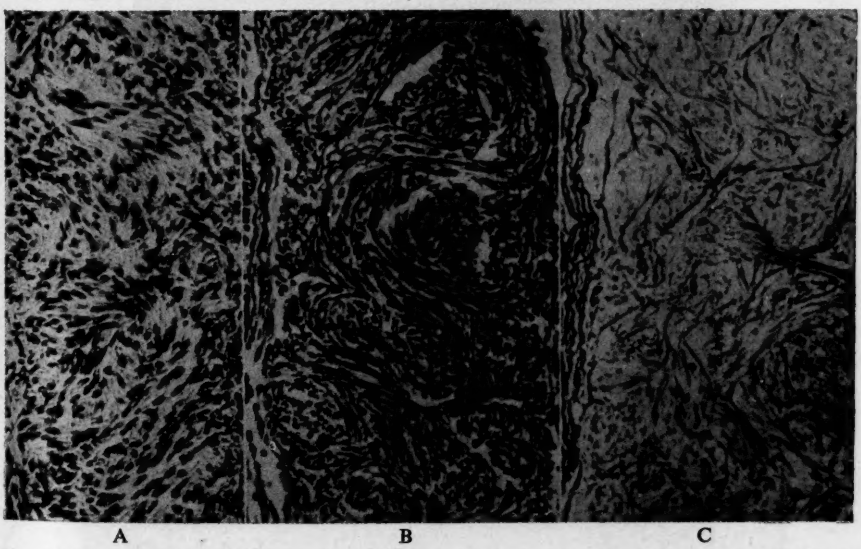

FIG. 4 (From Levin, 1952).—Regenerating fascicle in oculomotor nerve root with elongated cells and fibres arranged in interlacing bundles.

(A) Appearance with routine cell stain, showing palisading of nuclei; haematoxylin and eosin; ×165.

(B) Nerve-fibre preparation, showing prominent fibre component. At top of figure is a bundle of irregular, but otherwise intact, nerve fibres. Bodian; ×165.

(C) Reticulum preparation. Reticulin fibres are fewer and more delicate than axons. At the top the endoneurium is densely impregnated. Perdrau's modification of Bielschowsky's method; ×165.

of muscles are recorded electronically after tiny electrodes have been inserted directly into the muscle being examined. Electromyography provides proof of degeneration in some instances when there are no clinical evidences of it. When the nerve-muscle unit is undergoing pathologic change one can detect abnormal potentials, erratic firing, bursts of discharge, or rapid fatiguing. Examination of muscle activity by this technique supports the concept of misdirection of regenerated third nerve fibres. Björk (1954a, b) is the pioneer in this field, and in the United States Breinin is a leading authority.

Recently we have attempted such studies in an individual who probably harboured an aneurysm and had had a haemorrhage on one occasion. She exhibited clinical evidence of the misdirection phenomenon after third nerve paralysis and regeneration. This patient at rest had a complete ptosis, and some limitation of upward, downward, and medial gaze in the affected eye. The pupil was semidilated and fixed to light, but when an effort was made to direct the eye medially and downward, the upper eyelid retracted and the pupil narrowed (Fig. 5 A, B, C).

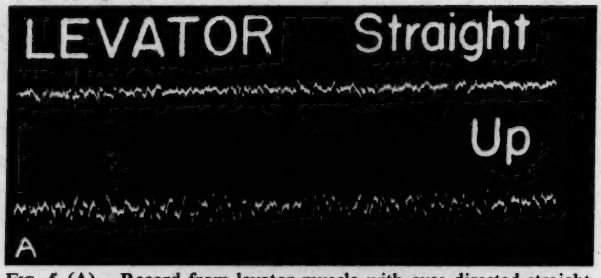

FIG. 5 (A).—Record from levator muscle with eyes directed straight forward. Action potentials are low but definitely present and appear quite regular. When an effort is made to look up, the action potentials become irregular and appear to discharge in bursts, indicating abnormal activity.

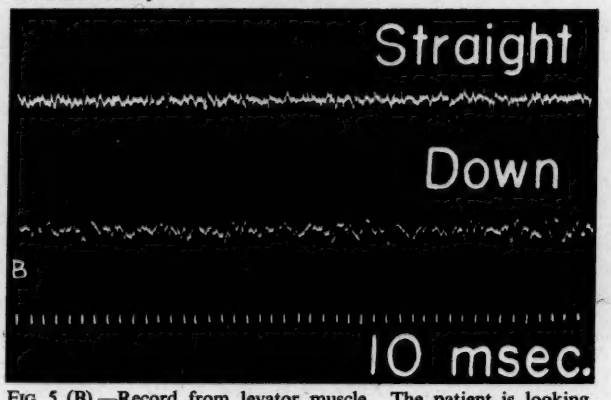

FIG. 5 (B).—Record from levator muscle. The patient is looking down. The activity in the levator is recognized.

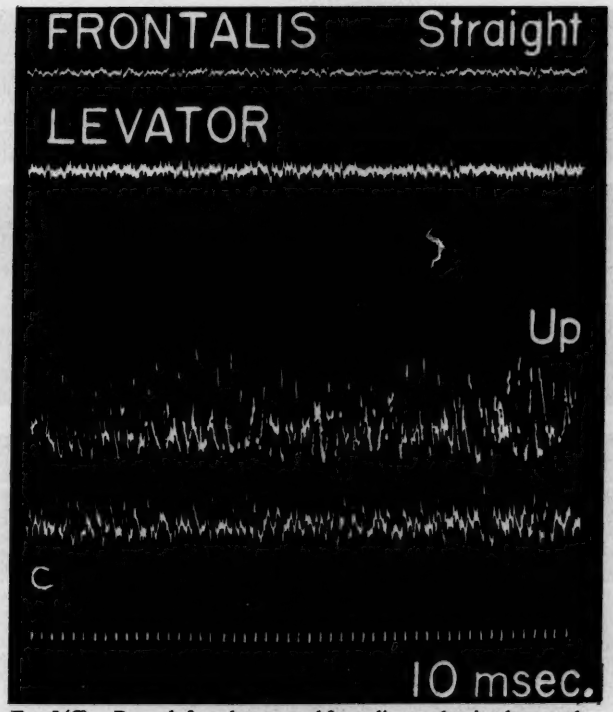

FIG. 5 (C).—Records from levator and frontalis muscles simultaneously. The patient was asked to look up. By far the greatest activity is seen in the frontalis, but there is increased, though rather irregular, activity in the levator.

Dr. G. M. Breinin has given me a great deal of help with the electromyography, and I am indebted to him for the case summaries and tracings which are reproduced below (Breinin and Moldaver, 1955).

Case Reports

Case 1, Diabetic Neuropathy.—A 72-year-old diabetic woman developed a total left third nerve palsy with orbital pain. The eye sat at the outer canthus but could be adducted almost to the midline. Peripheral polyneuritis was present. Very faint activity in the medial rectus was generated on adduction and no activity was present on abduction. A tiny remote unit was detected in the levator. No fibrillation was observed. The condition improved over a period of months (Fig. 6).

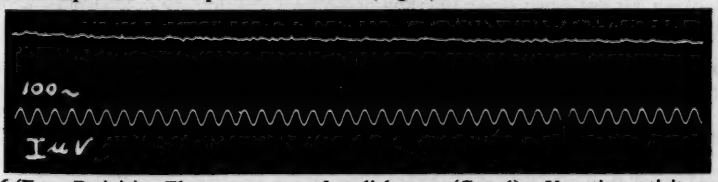

FIG. 6 (From Breinin).—Electromyogram of medial rectus (Case 1). Very tiny activity present.

Case 2, Probable Diabetic Neuropathy.—A 60-year-old man developed orbital pain on the right side. One week later an external third nerve paralysis developed with some retention of elevation and depression. This improved in 6 weeks. A glucose tolerance test was borderline. Electromyography of the right medial rectus showed slight activity in adduction with a tiny single unit firing. No activity was present in abduction. No fibrillation was observed (Fig. 7).

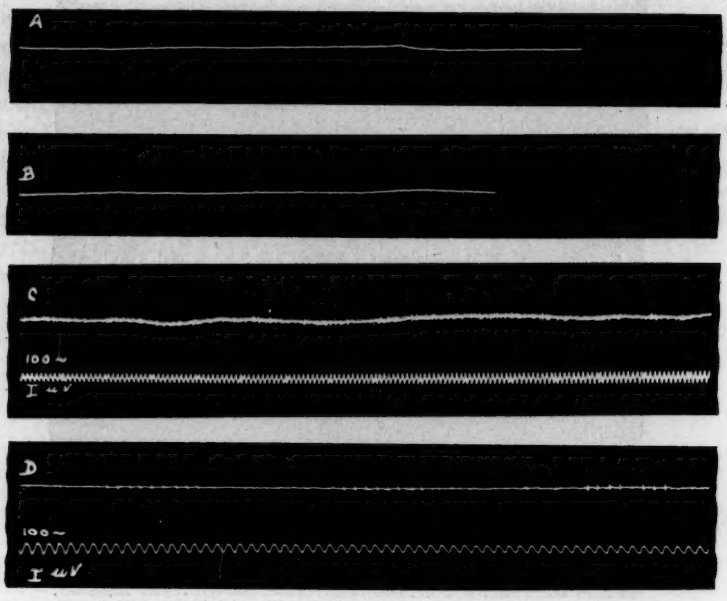

FIG. 7 (From Breinin).—Electromyogram of right medial rectus (Case 2).
(A) Abduction—no activity.
(B) Slight adduction—very faint activity.
(C) Maximal effort at adduction—tiny potentials.
(D) Adduction—runs of tiny single units.

Case 3, Diabetic Neuropathy.—A 60-year-old diabetic female developed a bilateral ptosis without other extra-ocular muscle involvement. Electromyography of the levator revealed no activity. The Tensilon (Edrophonium) test was completely negative (Fig. 8, opposite).

Case 4, Traumatic Third Nerve Palsy.—A 67-year-old man had had a traumatic left third nerve palsy 3 weeks before the examination. There was no electromyographic activity in looking left but much single unit and polyphasic unit activity in attempted adduction. Many of the units were of large amplitude (Fig. 9, opposite).

Case 5, Aberrant Third Nerve Regeneration.—A 30-year-old man suffered a traumatic third nerve palsy with a fractured skull; 4 months later adduction was good and elevation of 10°–12° was present but depression was very slight. The pupil constricted on adduction and widened on abduction. No lid retraction occurred. Adduction occurred on gaze up and down. Electromyography revealed simultaneous activity of the medial rectus, inferior rectus and inferior oblique on gaze up and down. The oblique recruited

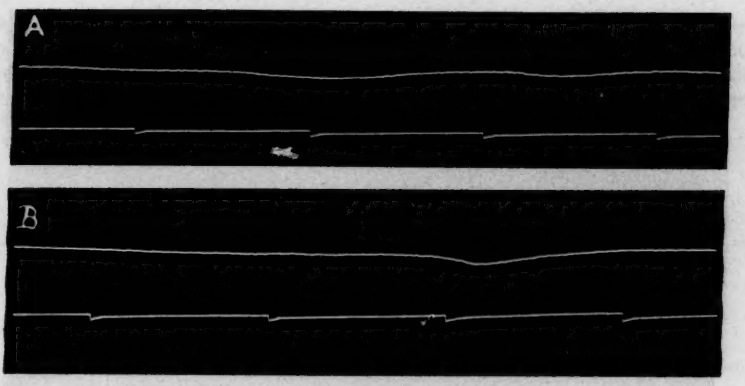

FIG. 8 (From Breinin).—Electromyogram of right levator (Case 3).

(A) Before Edrophonium } no activity.
(B) After Edrophonium }

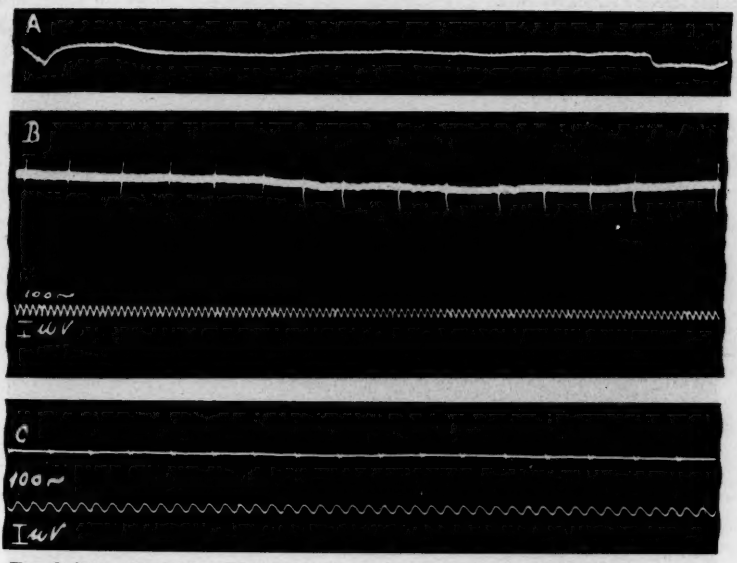

FIG. 9 (From Breinin).—Electromyogram of medial rectus, adduction in different electrode positions (Case 4).

(A) Tiny activity.
(B) Large polyphasic unit.
(C) Small polyphasic unit.

on adduction and was inhibited on abduction. The medial rectus also exhibited large activity in abduction (anomalous innervation). The aberrant process appeared to involve primarily the lower division of the oculomotor nerve (Fig. 10, *a*, *b*, *c*, overleaf).

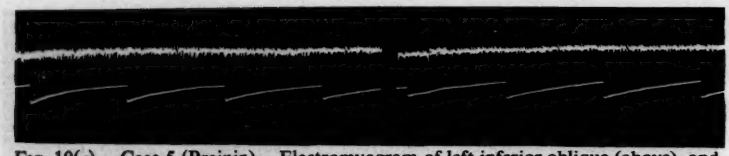

FIG. 10(*a*).—Case 5 (Breinin). Electromyogram of left inferior oblique (above), and integrator (below).

Fixing left up and in
Fixing right down and in } equal activity.

[The tracing shows proper activity on fixing left up and in. The activity on fixing right down and in should not be present unless there is misdirection.—F. B. W.]

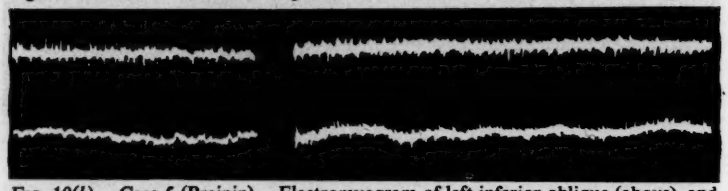

FIG. 10(*b*).—Case 5 (Breinin). Electromyogram of left inferior oblique (above), and left inferior rectus (below).

Fixing left down
Fixing right up } both active out of field.

[Upper left and lower right show abnormal activity and suggest misdirection.]

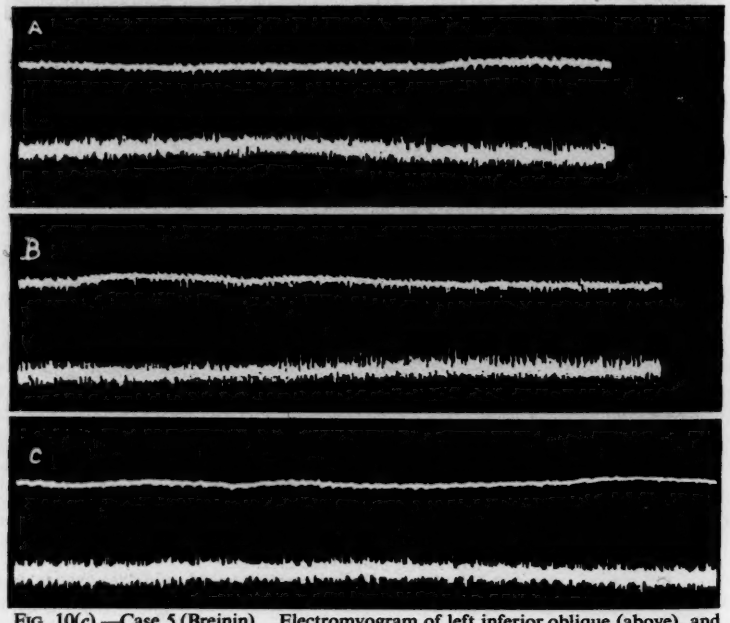

FIG. 10(*c*).—Case 5 (Breinin). Electromyogram of left inferior oblique (above), and left medial rectus (below).

(A) Primary position
(B) Adduction } both increase.
(C) Abduction—oblique inhibited while medial rectus increases anomalously.

Case 6, Traumatic Third Nerve Palsy.—A 17-year-old boy suffered a traumatic external third nerve palsy; 2 months later practically no vertical movement was possible but a good range of horizontal movement was present with fusion. Simultaneous activity was present in the medial rectus and inferior oblique. Very little activity was present in the inferior rectus (Fig. 11).

FIG. 11.—Case 6 (Breinin). Electromyogram of left medial rectus (above), and left inferior oblique (below). Both recruit from primary position to gaze up.

Case 7, Traumatic Third Nerve Paralysis.—The patient suffered a fractured skull in October, 1956. There was total paralysis of the right third nerve; 7 months later lateral movements of the eye were full but the eye could not be moved up or down. The right lid showed partial ptosis. It elevated sharply when the eye was adducted and to a lesser degree when an effort was made to look down. The pupil was fixed in mid-dilation (Fig. 12*a*, *b*).

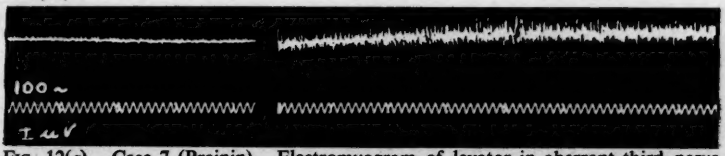

FIG. 12(*a*).—Case 7 (Breinin). Electromyogram of levator in aberrant third nerve regeneration Left—primary position. Right—adduction.

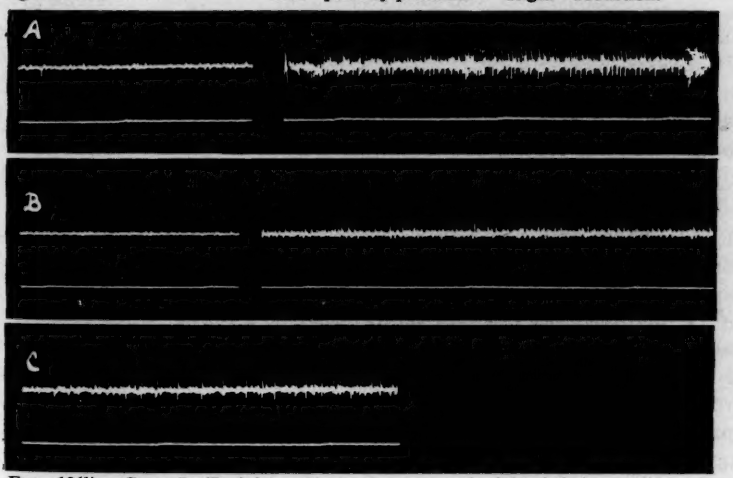

FIG. 12(*b*).—Case 7 (Breinin). Electromyogram of right inferior oblique in aberrant third nerve regeneration.

(A) Left—primary position. Right—adduction.
(B) Left—abduction. Right—elevation (attempted).
(C) Depression (attempted).

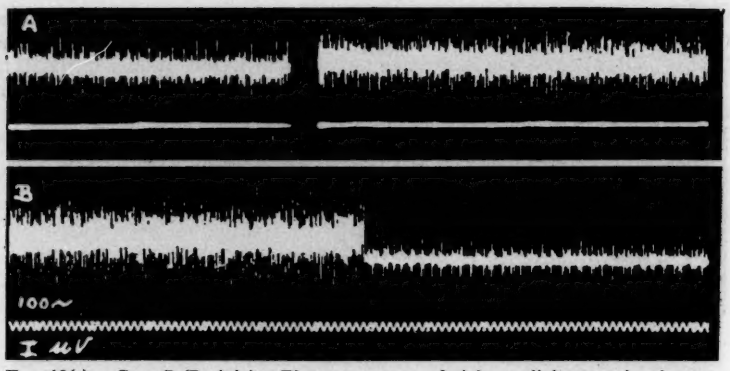

FIG. 12(*c*).—Case 7 (Breinin). Electromyogram of right medial rectus in aberrant third nerve regeneration.

(A) Left—primary position. Right—adduction.
(B) Left—elevation. Right—depression (attempted).

FURTHER CLINICAL STUDIES ON THE MISDIRECTION OF REGENERATED THIRD NERVE FIBRES.—In my private files I found the following records concerning third nerve regeneration:

17 patients with intracranial aneurysms;
14 cases of trauma;
4 cases of inflammation;
4 diabetics;
3 individuals who suffered from ophthalmoplegic migraine;
3 cases of intracranial tumour;
3 cases of undetermined aetiology.

In a great many instances patients with third nerve paralysis or paresis were seen only once or during a short period and in consequence they offered nothing as regards regeneration.

Cases of acquired third nerve paralysis may be divided into two groups:

(1) Those with no evidence of the misdirection of regenerated fibres;
(2) Those in which such evidence is apparent.

(1) Acquired Third Nerve Paralysis without Misdirection

(*a*) *Diabetes.*—My series of four cases showed what is now generally well known: individuals with diabetes of long-standing may develop third nerve paralysis (Waite and Beetham, 1935; Weinstein and Dolger, 1948). In many instances diabetics who exhibit third nerve paralysis have complained of severe pain at the onset; furthermore, the pain is likely to have had the precise distribution of that which regularly characterizes anteriorly situated aneurysms. In consequence, when an individual with diabetes develops a third nerve paralysis aneurysm is suspected. Cogan (1956) suggested that

some vascular process explains the pain. Often the diabetes is of long-standing and in many cases a retinopathy is present.

I have observed one patient in whom there was a third nerve paralysis first of one, and then of the other eye. This case was reported by Eareckson and Miller (1952). Aneurysm was suspected but arteriography showed nothing remarkable. Within a matter of several weeks there was a complete recovery without evidence of misdirection of regenerated fibres. Then third nerve paralysis with sparing of the pupil made its appearance on the opposite side and again the pain was precisely that which occurs with aneurysm. Within a few weeks there was complete recovery from the third nerve paralysis. The case is particularly noteworthy in that, although all the extra-ocular muscles were paralysed, there was total absence of internal ophthalmoplegia in each eye.

An explanation for third nerve paralysis in diabetes has been conjectural since its first description in 1866 (Dreyfus, Hakim, and Adams, 1957). Peripheral neuritis comes to mind, but it seems unlikely that such an involvement would be unilateral as usually occurs.

An opportunity to do a *post-mortem* study enabled Dreyfus, Hakim, and Adams to present us with histopathological evidence.

Their patient was a 62-year-old woman who was known to have had diabetes for 10 years. Probably the diabetes was poorly regulated. Five weeks before admission to hospital she developed left ptosis with left-sided headaches which persisted. The left eye could not be adducted beyond the midline and vertical movements were very slight. Ptosis was complete, but the pupil was spared. In order to rule out an aneurysm a left carotid arteriogram was made. After a short time the patient died.

Dreyfus, Hakim, and Adams found a fusiform enlargement of the left third nerve in the retro-orbital (intracavernous) portion of the third nerve with the enlargement affecting approximately one centimetre of nerve. Principally centrally there was destruction of some of the axons and myelin sheaths. There was an increase in the connective tissue of the nerve and a suggestion of regeneration in the area of destruction. There was Wallerian degeneration in the distal segment of nerve and minimal evidence of axonal reaction in the left third nerve nucleus.

This autopsied case characterized by pupillary sparing is of interest in regard to the description of the pupillomotor fibres occupying a superior and peripheral position in the nerve between the cavernous sinus and the midbrain (Sunderland, 1952). Sparing of the pupil in diabetic third nerve paralysis has additional interest when it is recalled that in diabetics there is occasionally encountered a pupil which is rigid to light and in some instances cannot be differentiated from an Argyll Robertson pupil. With third nerve paralysis associated with aneurysm, trauma, or tumour, the pupil is almost invariably involved. I recall having had a case of aneurysm and a case of tumour in which third nerve paralysis was complete except in that the pupil was completely spared.

Dreyfus, Hakim, and Adams (1957) injected Neoprene (a polymer of chloroprene) into the basilar and carotid arteries of cadavers in order to study the blood supply of the third nerve. They found small arteries arising from the posterior cerebral or superior cerebellar arteries entering the nerve where it passes between these arteries. At the orbital end of the nerve they

demonstrated the blood supply to the nerve from the ophthalmic artery. They were unable to demonstrate the blood supply to the intracavernous portion of the third nerve. They suggested incomplete ischaemia as a possible cause of diabetic third nerve paralysis.

It seems significant that the misdirection phenomenon occurs so rarely with diabetes where there is third nerve paralysis. In these cases recovery from paralysis begins earlier than when the paralysis is due to aneurysm or trauma. Cogan (1956) stated that, if there is recovery from oculomotor paralysis within 6 weeks, aberrant regeneration does not occur. In the autopsy report by Dreyfus and others (1957), the completeness of the paralysis with the incomplete involvement of the nerve was commented upon. Dreyfus, in a personal communication, stated that he had not seen any report of aberrant regeneration in diabetics with third nerve palsy. Also, he remarked that he saw no reason why such regeneration should not develop after a lesion. The almost total absence of response to electromyography in these cases during the earlier stage is of interest (Figs 5, 6, and 7).

(*b*) *Ophthalmoplegic Migraine.*—This affection, which may be characterized by third nerve paralysis, is seen infrequently. In each of my three patients who seemed to qualify for this diagnosis, there were several attacks of third nerve paralysis. In one, a child aged 12, there was a history of recurrent headaches associated with third nerve paralysis commencing at 3 years of age. When we observed him he had had his sixth attack and the third nerve paralysis on the right seemed complete. In these cases total third nerve paralysis including pupillary involvement seems to be the rule. Recovery from the paralysis commences within a few weeks at the most and is always complete so far as I am aware. There has been no evidence of misdirection of fibres in my cases or in any others that I know about.

Harrington and Flocks (1953) recently suggested that herniation of the temporal lobe is a mechanism which may explain ophthalmoplegic migraine. While this idea may have merit certainly the mechanism has not been established. It is of interest that the herniation of the temporal lobe occurs very often with chronic subdural haematoma and certainly in this circumstance total third nerve paralysis is exceedingly uncommon.

In the cases which I have included under ophthalmoplegic migraine, aneurysm seems to have been eliminated in all instances, and in this regard the absence of misdirection of regenerated fibres has importance.

(*c*) *Temporal Arteritis.*—I had no patients in this category, but Murray (personal communication) has observed third nerve paralysis in a 66-year-old woman who was shown by biopsy to suffer from temporal arteritis. On the side of the involvement she developed a total third nerve paralysis excepting that the pupil was spared. Within 6 weeks recovery from the paralysis was almost complete and there was no evidence of misdirection.

(2) Acquired Third Nerve Paralysis with Misdirection

(*a*) *Intracranial Aneurysm.*—Aneurysms situated at the base anteriorly are characterized by a symptomatology which is generally well known. Often there is pain in the temporofrontal region with or without loss of consciousness, and frequently blood is found in the spinal fluid. If, in addition, there is a third nerve paralysis, the diagnosis of aneurysm is almost a certainty. The onset of third nerve involvement varies widely. In many instances, evidence of the onset of oculomotor paralysis occurs within a matter of hours after the onset of pain but in some instances the nerve palsy may appear days, or even weeks, after the initial signs. In both circumstances the third nerve paralysis in these cases is likely to become complete with a dilated and fixed pupil. It seems obvious that the third nerve paralysis may result from pressure, from interference with blood supply to the nerve, or from intraneural haemorrhage. Which of these factors is responsible usually is not established. As regards regeneration of the paralysed nerve, it can be said with assurance that it usually develops and that evidence of misdirection of fibres is almost invariably present. However, I have seen in an individual with a proven aneurysm a third nerve paralysis which remained total and unchanged 10 years after the diagnosis was established.

The misdirection phenomenon may be fully or only partially developed. In some instances the picture varies widely from that which has been described herein as classical. Instead of regenerated fibres being fairly generally distributed to the muscles, an uneven distribution may account for bizarre ocular movements. Cogan (1956) remarked upon such an unusual circumstance. He stated that, if the levator muscle receives fibres originally connected with the superior rectus muscle, the eyelid rises with normal voluntary upward movements of the eyes and also with involuntary upward movements (Bell's phenomenon) on attempted closure of the lids, and at other times the affected eyelid shows ptosis. "In other words, the lid opens widely when an attempt is made to close it" (Fig. 13).

FIG. 13.—There has been left-sided third nerve paralysis (Gifford, 1939; see Cogan, 1956).
(A) Left upper lid partially elevated by contraction of frontalis.
(B) Ptosis on left is nearly complete.
(C) Paradoxical elevation of left upper lid during closure of right eye.

A remarkable situation is shown in Fig. 14 (Bielschowsky, 1935). In this patient, efforts to look up resulted in the affected eye turning sharply downward. Probably, in the affected eye regenerated fibres had failed to reach the superior rectus muscle and were concentrated in the inferior rectus. Bielschowsky's explanation in this particular case was that the downward movement was produced through the action of the fourth nerve; this seems unlikely and the regeneration syndrome is probably the proper answer.

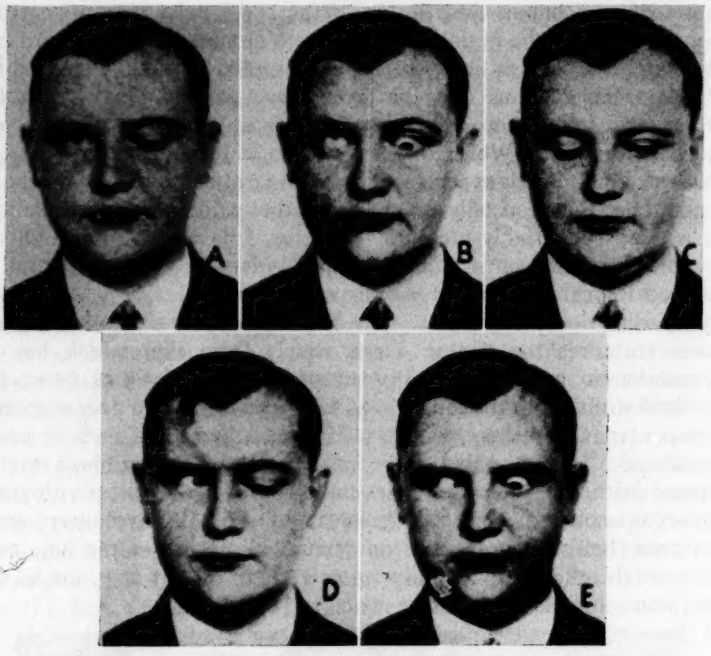

FIG. 14 (Bielschowsky, 1939).

(A) Left oculomotor paralysis with left upper lid completely relaxed.
(B) Maximum contracture of left superior oblique prevents left eye from reacting to elevation impulse, the left upper lid being raised considerably.
(C) Maximum innervation of depressor muscle causes slight lifting of upper lid.
(D) Laevoversion impulse, with complete relaxation of left upper lid.
(E) Dextroversion impulse, with maximum retraction of left upper lid.

Incomplete syndromes occur not infrequently. Elevation of the upper eyelid (the so-called pseudo-Graefe sign) is certainly the most early recognized manifestation of the syndrome. In the case reported by Levin (1952), it was the most prominent evidence of the regeneration process (Figs 3 and 4). Not uncommonly there is some limitation of adduction. Vertical movements may be present in some degree, and I think that upward movement is

more likely to be abolished with incomplete syndromes than downward movement.

Probably sufficient has already been said regarding the pupil. I have no case record in which an Argyll Robertson type of pupil has been the sole remaining evidence of the misdirection of regenerated fibres in a case of third nerve paralysis. In all likelihood such cases exist.

(*b*) *Trauma.*—There is nothing about the syndrome of regeneration in these cases that differs from that observed in association with aneurysm, excepting that with trauma the paralysis occurs immediately. After trauma the syndrome may be classical and complete, including changes in the pupil, or it may be incomplete. In my fourteen cases there were included two attributed to birth trauma, and in one of these the syndrome was complete.

Traumatic third nerve paralysis not infrequently becomes a medico-legal problem. I have had experience with three such cases, in all of which the syndrome was complete. In each one it was accepted that from the practical standpoint the injured eye was lost (visual acuity in all three was excellent) because of the diplopia present in all fields.

(*c*) *Intracranial Tumour.*—It has been difficult for me to understand how rarely misdirection of regenerated third nerve fibres occurs in association with cerebral tumours. A child aged 7 exhibited third nerve palsy as an early evidence of pituitary tumour, and after operation a classical misdirection syndrome developed.

(*d*) *Inflammation.*—In three of four patients who exhibited the syndrome as a result of inflammation, there was a history of treated syphilis. The fourth, a child aged 2, obviously suffered from septic cavernous sinus thrombosis. The blood culture was positive. The child was the first youngster in the Harriet Lane Home to receive sulpha drugs. He made a remarkable recovery, but developed a classical misdirection syndrome.

(*e*) *Undetermined Aetiology.*—My three cases in this category were not remarkable. In none was there pupillary change.

It is opportune to remark here that we have observed a 14-year-old Negro boy who was admitted to hospital because of unilateral ptosis, said to have been present since birth. He exhibited a unilateral jaw-winking (Marcus Gunn) phenomenon. There was a double elevator palsy on the side of the ptosis. When the eye was adducted, the upper lid was sharply elevated. The elevation of the upper lid could have been explained on the basis of misdirection of regenerated fibres. It seems possible that both syndromes were present in this patient.

Prognosis and Treatment

When regeneration has developed, there is no possibility of the signs of misdirection disappearing spontaneously.

In the fully developed syndrome, surgical therapy cannot possibly provide

single vision and free motility of the affected eye. In occasional instances, as for example when a ptosis has persisted, a surgical procedure may be employed to advantage.

SUMMARY

Regeneration of the third nerve in some instances is associated with abnormal ocular and lid movements. In the fully developed misdirection syndrome, a fairly constant pattern of abnormality is seen. Our present knowledge concerning the misdirection syndrome is outlined: usually there is evidence of misdirection when the third nerve paralysis has been associated with aneurysm or trauma; it is less frequent when it is the nerve that has been affected by intracranial tumour or inflammation; it does not occur when third nerve paralysis results from ophthalmoplegic migraine or diabetes. Once the regenerating nerve fibres have taken the wrong course there is no likelihood of the condition regressing spontaneously. Surgical treatment may be of value in cases of persistent ptosis.

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SOME OBSERVATIONS ON THE PUNCTATE KERATIDES IN AFRICA*

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THE "keratitis punctata superficialis" described by Fuchs (1889) is better known to-day as epidemic virus kerato-conjunctivitis. (The nummular keratitis of Dimmer is almost certainly a variant of it.) It has been reported in epidemic form from Europe, America, Tasmania, India, China, Japan, Java, Malaya, Hawaii, and Canada, and in all these countries sporadic cases are the rule. The position has been excellently reviewed by Hogan and Crawford (1942). The disease was found to be so common during the course of a recent ophthalmic survey carried out in British West Africa that there can be little doubt it is widespread in the African continent also. In this part of the world, however, the differential diagnosis is complicated by certain tropical diseases, especially onchocerciasis, all of which have a serious prognosis. Because of this, the present study was started in the hope of finding some clear-cut differences in the clinical pictures to help in diagnosis.

I. DIFFERENT TYPES OF PUNCTATE KERATIDES

The clinical picture of epidemic kerato-conjunctivitis is well described by Cockburn (1954). A claim was made that the causative virus was isolated by Sanders and Alexander (1943), but it has recently been suggested that the aetiological agent is Type 6 of the group of adenoid viruses (Jawetz, Kimura, Nicholas, Thygeson, and Hanna, 1955). It should be noted that trauma increases the susceptibility of the eye to infection (Viswalingam, 1941). While the characteristic lesion is punctate in form, involving Bowman's zone, coalescence may lead to larger opacities of variegated shapes and their appearance in the interstitial stroma is by no means rare. Relapses are common.

An acute punctate kerato-conjunctivitis closely simulating the epidemic type is the most common manifestation of herpes febrilis keratitis. The well-known dendritic keratitis, which the writer found very common in India, was seen only twice in some 5,000 cases of eye disease examined in Africa. Disciform keratitis also appears but rarely. Characteristically, the punctate

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lesion is recurrent and associated with fever. Corneal anaesthesia is an invariable accompaniment. Infection of the cornea is also said to be facilitated by minor epithelial injuries. Fluorescein stains the lesions only early in their course. This picture, apart from corneal anaesthesia, is clinically identical with the epidemic virus keratoconjunctivitis, even as far as the distribution and appearance of the opacities go.

Punctate corneal opacities of the same type occur in the tropics in trachoma, leprosy, and onchocerciasis. Trachoma and leprosy may be quickly dismissed, because in the first disease the opacities are always associated with an active and unmistakable pannus trachomatosus, and in the second they are accompanied by the easily diagnosed signs of either nodular or anaesthetic leprosy, especially the latter. Superficial punctate keratitis is not the most common feature of ocular leprosy in Africa nor—and in this we are in agreement with Barros (1939)—is corneal anaesthesia a prominent finding when the keratitis is present. Apart from the obvious cutaneous signs of the disease, leprous opacities do not stand out in a clear cornea as in the epidemic cases, but lie within a grey veil of corneal infiltration as in trachoma. Moreover the opacities are very small (0·25 mm.). For these reasons the pictures should not readily be confused.

The one tropical disease which has been said exactly to simulate virus kerato-conjunctivitis is ocular onchocerciasis. Luna (1919) first described a chronic form of punctate keratitis which he unhesitatingly ascribed to the activities of the parasite, claiming that the picture was specific, although admitting that the corneal lesions were somewhat similar to those described in Europe by Fuchs. Luna's description showed the lesion to commence with acute photophobia and lacrimation and a smarting pain, which soon settled. The lesion then ran a chronic course. Nodules were present, and on this evidence alone the condition was considered to be due to onchocerciasis. His view was lent much support, however, by his claim that subsequently the classic picture of an onchocercal anterior uveitis supervened.

Hissette (1937) stated that he does not agree with Luna that this lesion is specific. He considers it to be in all respects similar to other types of secondary punctate keratitis. He mentions leprosy and trachoma as examples of the latter, the punctate corneal lesions being classified as "epiphenomena". At the same time, he recognizes the existence of many cases of a primary punctate kerato-conjunctivitis in Central Africa, similar, he says, to those described by Herbert and Kirkpatrick in India. He classifies the punctate keratitis of Fuchs as secondary, on the grounds that the lesion spreads from the conjunctiva. The epidemics described by Fuchs (1889) and by Herbert (1901) and Kirkpatrick (1920), nevertheless, are now all known to be classical examples of epidemic virus kerato-conjunctivitis. The value of Hissette's somewhat involved arguments lies in his later statement that with the slit lamp he could see microfilariae dying

in the cornea, and exudations forming around them. He does not enlarge on this.

Ridley (1945) is another who observed (on one occasion) an opacity forming around a dead microfilaria in the cornea. He states that the lesion is specific and primary. He describes the opacities as lying below Bowman's membrane in the stroma in the lower half of the cornea, especially nasally. Their size, he says, is about 0·6 mm. in diameter, their colour is grey, and they are nummular in shape, with ill-defined edges. Within recent lesions, according to this worker, the dead body of a microfilaria may be seen (presumably by slit lamp) lying straightened out in a horizontal direction. The appearances of the two corneae, Ridley goes on to say, are usually strikingly similar. The whole condition is a quiet one, without signs of corneal vascularization. In short, Ridley shows the punctate keratitis of onchocerciasis to be an avascular nummular interstitial keratitis, the origin of which depends upon the formation of opacifications around dead microfilariae. This is the generally accepted view to-day. As such, there appears to be very little difference indeed between this clinical picture and those of the punctate keratitis due to the herpes and the epidemic viruses, except in the level at which the opacities are found. Here Ridley disagrees with Hissette, who believes them to lie on either side of Bowman's membrane, and the present writer confirms Hissette's observations. As, after all, the distinction is one of a very fine degree only, it would seem that some other argument must be found if these three conditions are to be distinguished one from the other.

In passing, Greeley disease should be mentioned. This lesion, described recently by Cockburn (1953), is a punctate keratitis associated with muscle pains and pharyngitis. It may prove in the end to be due to a variant of the epidemic-type virus. To date no other cases have been reported.

II. Clinical Description of the Three Main Types of Punctate Keratides seen in 750 African Subjects

Of 750 cases of eye disease (of mixed origin) in an endemic onchocerciasis area, 300 had microfilariae in the conjunctiva and 450 had none.

Of the 450, 302 had positive skin biopsies, and the other 148 did not suffer from onchocerciasis at all.

Of the 300 with positive conjunctival biopsies, 160 had corneal lesions due to onchocerciasis; of these 160, 22 exhibited punctate keratitis associated with onchocercal sclerosing keratitis, and 27 with a limbitis. Of the 140 with positive conjunctival biopsies but no signs of onchocercal keratitis, 33 exhibited corneal opacities.

Of the 302 with positive skin biopsies but negative conjunctival biopsies, twelve exhibited corneal lesions associated with corneal opacities, and thirty had corneal opacities alone. Of the 148 who did not suffer from

onchocerciasis, 29 exhibited corneal opacities, none being associated with any other corneal lesion.

It may be assumed from these figures that the 22 cases of corneal opacity associated with a characteristic onchocercal sclerosing keratitis should illustrate features typical of the punctate keratitis of onchocercal origin and may be compared with the 29 cases not suffering from onchocerciasis. One is still left of course with those cases of corneal opacity in which microfilariae are present in the conjunctiva but are not associated with any other sign of onchocercal ocular disease; they will be considered later.

(a) Punctate Keratitis of Onchocerciasis.—It is possible, although perhaps theoretically unlikely, that an avascular nummular interstitial keratitis (Ridley's term) may occur in the absence of other ocular lesions. The parasites enter the cornea at the limbus, usually from the sub-conjunctival space, and one would expect them to produce changes either in the conjunctiva or at the limbus before or simultaneously with any change appearing in the cornea. Neither Ridley nor Hissette mention this, although it must be said that most of the excellent drawings of the latter illustrate it. This has to be emphasized, in our view, right at the outset. The appearance of these corneal opacities associated with the characteristic sclerosing keratitis of onchocerciasis (22 cases) was as follows:

Their size varied greatly from 0·25 to 2 mm. in diameter. Their colour was usually densely white or yellow. They did not stain. Their position in the optic section was nearly always the same: they invariably invaded Bowman's zone as well as the lower layers of cells in the epithelium; in advanced cases they were found at a deeper level in the stroma, though this was rare and the term "superficial" appears to be preferable. The opacities were round or polyhedral in outline. They were situated in close relation to the protruding tongues of pannus onchocercosus, fairly frequently in one eye only; as the pannus was almost always found in the lower half of the cornea, usually commencing at 3 and 9 o'clock, the punctate opacities sometimes intruded on the pupillary area; we seldom saw them in the upper cornea. As might be expected they were accompanied by lacrimation and photophobia; the discharge was clear and watery. There is some doubt in our mind whether these opacities originated as a result of reactions around the dead bodies of microfilariae, for we have no histological evidence of it; on several occasions, such opacities were excised and stained, but no microfilariae were found; using a very high magnification we have on occasion seen living microfilariae moving in the vicinity, but that is the most we can say. (This will be discussed later.) The acute onchocercal keratitis associated with punctate opacities frequently quietens down without treatment, and there may be some consequent clearing of the opacities; but, even when such a state of affairs exists in a quiet eye, the condition is usually easy to diagnose, as the pannus onchocercosus seldom resolves to any extent at all; it is more difficult to be certain in the case of a limbitis, as this frequently resolves quite considerably. In the active stage, however, there is little doubt.

(b) Epidemic Type of Punctate Keratitis.—The characteristic picture in Africa of this condition was observed over an 18-month period in eleven of the 29 subjects exhibiting this lesion within the main group of 750 cases. None of these patients was suffering from onchocerciasis. At its simplest, the condition showed itself as an acute hyperaemia of the conjunctiva, followed in a few days by lacrimation, and after a few days more by the appearance of the punctate opacities. Lacrimation was the rule, and photophobia very common; the discharge was usually clear and watery, although in one-fifth of the cases it was sticky and white at some stage in the illness. No distinctive bacillus—such as Morax-Axenfeld—was isolated. The discomfort was invariably bilateral, although the appearance of the punctate opacities was not infrequently restricted to one eye. A mild folliculosis and a slight chemosis of the lower fornix occurred in one-third of the cases, but was transient and lasted only about a week. The feeling that a foreign body lay under the lids was usual, and a sore throat was occasionally a symptom. Defective vision, when noted, was always due to invasion of the pupillary area of the cornea by the opacities. The attacks were always fairly mild. (The most severe attacks were seen in a few expatriate Europeans apart from the members of this group.) The characteristic sensation was one of discomfort, not pain. After the acute phase, which lasted from 2 to 3 weeks, the condition settled down to a long period of chronicity, punctuated by slight relapses, at something like 3-monthly intervals in the majority of cases. In its chronic phase, slight lacrimation alone was observed; however, with interference at examination, a hyperaemia of the bulbar conjunctiva quickly commenced; in short, the conjunctiva was readily irritated. Some cases healed spontaneously within a year; others were still active at the end of 18 months.

Objective examination revealed that a mild degree of hypo-aesthesia existed in the region of the opacities, but this was never as complete nor as constant as that which occurred in herpes febrilis keratitis. At no time did we observe conjunctival haemorrhages nor membrane formation. Preauricular adenitis occurred in most cases, but as this is very common in Africa (because of lice, scabies, etc.) little diagnostic significance can be attached to it. From the start of these studies, specific descriptive terms for the different appearances of the corneal opacities were used, with a view to discriminating between possible stages in their development from onset to resolution and between the punctate opacities of the epidemic type of lesion now under discussion and those associated with onchocerciasis and herpes febrilis. Only the three most common will be described below.

The newly formed opacity, from 0·25 mm. to 1 mm. in diameter, looks like a "morula", that is to say the opacity consists of a round collocation of regularly-spaced grey flecks; in its last appearance the opacity is of the same diameter but has become uniformly grey in colour; it is like a "patch". Several intermediate variations were seen. Over the 18-month period of the observations, recovery

was invariably shown to be accompanied by a shift from the morula type to the patch type. Many such patches were subsequently seen to diminish in size, usually clearing first in the centre to form a "halo", so it seems likely that of those finally disappearing all went through this morphological change. This helps in the prognosis. It takes about 6 months for this to happen and about another 3 for the subsequent patch to fade if it is going to fade. Where opacities remain after a year, it seems they are most unlikely ever to disappear, even if the configuration has changed from morula to patch. Where the number of opacities was great (forty or sixty) in a severe attack, they had a distinctive appearance. They were smaller, 0·25 mm. on average, and are best described as looking like asterisks. In fact, they could be seen under high magnification to be small morula-types. They were yellowish-white and apparently the colour never altered, even when they were found to be diminishing in size before disappearing. One cannot help wondering if this picture may not be caused by a more virulent strain of virus.

As a rule, there were seldom more than six opacities in any one cornea; frequently there was only one. They were most frequently situated centrally or paracentrally, but, where the number was great, they spread over the entire cornea. All cases in the present group which had more than three attacks in a year showed an increase in the number of opacities when seen at the end of the period of observation. This, of course, to some extent depended upon the date of the last relapse or attack. In only three of the eleven cases examined did all the opacities present disappear; persistence is therefore to be expected, the average number of persistent opacities in the present study being three divided between the two eyes. This picture was seen time without number in healthy African eyes outside the main group of 750 in this paper, thereby giving us some idea of how widespread the disease is.

The corneal opacities are usually situated in Bowman's zone. As a result, there may be permanent damage to the superficial surface of the corneal stroma. Seen by the ocular biomicroscope, this zone forms the second relucent line, and must be regarded as part Bowman's membrane, part superficial corneal stroma. It is not surprising, therefore, that residual opacities are so common. The opacities were also found on occasion lying entirely in the epithelium or in the interstitial layers deep to Bowman's zone. Picked out quickly by the method of sclerotic scatter, they can be localized best in optic section by means of a very narrow beam. The larger ones were often seen to be saucer-shaped. The opacities nearly always remained isolated, and it was only rarely that fusion of two or three adjacent ones was observed. They were not always exactly round. None of them stained with fluorescein, which suggests that the health of the epithelium is not appreciably lowered. While only eleven such cases were observed over a period of 18 months, 56 other acute cases were noted in our later records, the clinical appearance of which agreed in every particular. This was also true of another group of thirty cases followed over a period of 9 months.

(c) Punctate Keratitis of Herpes Simplex.—It has already been said that the dendritic form of this disease is extremely rare in Africa. The disciform manifestation of herpes simplex (or febrilis) keratitis cropped up at regular

intervals during the course of the survey. By far the most common manifestation, however, is the punctate kerato-conjunctivitis, which at first appearances looks so like the epidemic type. Eighteen cases were examined over a 15-month period, and many others were observed for shorter periods during the survey. While it is fundamentally true to say that the two virus keratides present identical clinical pictures, there nevertheless emerged in all our herpes febrilis cases two constant factors not present in the epidemic type of punctate keratitis.* The first of these was the presence of an almost constant corneal anaesthesia, the second was the presence of at least one larger polyhedral opacity among the other opacities. In the epidemic type it is a hypo-aesthesia rather than an anaesthesia, and some times not even that; the corneal opacities moreover are always nearly round. These two findings, taken in conjunction with the history of an initial attack of fever (not reported clearly in every case, one must admit), make a diagnosis of herpes febrilis keratitis very probable. Where the diagnostic demonstration of increasing antibody titre during the first weeks of the illness is impossible, it must be admitted that even such minor diagnostic pointers are of some importance. Unlike the epidemic type, new attacks were common. The position of the opacities in the beam was identical for the most part with those seen in the other two diseases, except that deeper interstitial opacities (outside Bowman's zone) were never noted.

III. Discussion of the Aetiology of Isolated Corneal Opacities in the Quiet Eye

The problem posed by the presence of a few "morula", "halo", or "patch" type corneal opacities in a quiet eye, despite what has been said, remains. True, in the absence of nodules, of positive conjunctival and skin biopsies, of any evidence of atrophy of the skin, and of residual ocular onchocercal lesions, onchocerciasis as an explanation is unlikely. Even where the conjunctival biopsies contain parasites in a quiet eye, nevertheless, the observer is no further forward. It must be remembered that, in the present survey, the virus punctate keratides were very common in endemic onchocerciasis areas.

As we have seen, out of 148 subjects not suffering from that disease in an endemic onchocerciasis area, eleven exhibited the punctate keratitis of the epidemic type and eighteen exhibited herpes febrilis keratitis. Where the opacities are due to onchocerciasis, the whole condition may settle down and some resolution occur; in this event the final appearance may simulate that due to the two virus diseases. Where then, as has been said, the conjunctival biopsies are positive, and punctate opacities are present, even with co-existing evidence of an onchocercal sclerosing keratitis, one cannot say dogmatically that the punctate opacities have been due to any one of the three lesions under discussion. The high incidence of the virus keratides

* The average size of the opacities in recent epidemics due to the adenoviruses appears to have increased, approximating even more closely to that found in herpes febrilis.

in Africa is more convincingly illustrated by our observations in non-endemic areas; in a group of 120 Africans attending a teacher's training college, 41 were found to have corneal opacities of the type under discussion. None of them had onchocerciasis. Sixty per cent. of those with opacities had a history of an attack of fever during or immediately preceding their eye trouble, and only 38 per cent. of those without opacities in the group gave such a history. In another series of 100 young men and women, 23 had corneal opacities, and only one suffered from onchocerciasis. While we have not stressed the association of enlargement of the multifibre corneal nerve bundles in herpes febrilis keratitis, inasmuch as this observation is so open to human error, such an enlargement existed in our view in one-third of the first group and in one-half of the second. Malaria is such a commonplace in the tropics that it is easy to lose sight of the fact that despite his degree of immunity, the African also suffers from it. In a questionnaire issued to the training college mentioned above, this subject was investigated, and the answer showed that on the average a young African will have two or three attacks of fever every year (2·7). When dealing with African populations, it is important to remember that relapses of malaria occur for the greater part during the rains, which fall from May to September on the West Coast. Corneal opacities due to herpes febrilis keratitis may then be expected during this period; knowing as we do that they take from 6 to 9 months to disappear (apart altogether from the fact that a few opacities usually persist and that recrudescences are the rule), it can be seen that opacities from this cause alone will be present during every month in the year. It is not surprising, therefore, that their incidence is so very high. Distinguishing the two virus types on the basis of what has been mentioned above, in six cases of corneal opacity in African subjects, three according to our records will be due to the herpes virus, two to the epidemic type, and one to onchocerciasis.

With high magnifications we have studied the activities of microfilariae in the corneal tissue on many occasions, but have never had the good fortune to observe an opacity forming around a motionless one. On two occasions a living parasite was excised within its segment of corneal tissue, and was subsequently observed under the microscope in physiological saline; both were seen to crawl between the basal epithelium and Bowman's membrane, though they found it difficult to move, having to struggle violently in forcing a passage. It has already been noted that even minor epithelial trauma may precede the virus punctate keratides, and it is not beyond the realms of possibility that activities as forceful as those observed may produce just this state of affairs; in short, even when a characteristic onchocercal lesion of the cornea exists, because of the activity of the parasites in this tissue, an attack of one or other of the virus keratides may be precipitated. The vestigial space between Bowman's membrane and the epithelium through which the microfilariae pass is traversed by the delicate end-fibres of the

corneal nerve plexuses, which, it would seem, must be particularly vulnerable to this sort of attack. We mention this as another possible explanation of the lesions.

It has been pointed out that opacities sometimes resolve on administration of Hetrazan, and that when they appear again some months later, the conjunctival biopsies are found once more to be positive. At first sight such an association might seem a straightforward one. Theoretically, the filaricide by killing any other microfilariae in the cornea should increase rather than decrease the number of opacities, provided the pathogenesis of these lesions in the quiet eye depends upon the presence of their dead bodies, which, as indicated already, we doubt. The re-association of live microfilariae and punctate opacities certainly seems significant, and if correct must cast some doubt on the theory of the pathogenesis of onchocercal punctate keratitis.

Appelmans (1946) suggested that the latter might be an allergic reaction due to the hypersensitivity of the corneal tissue to the parasites. There is to date no evidence in support of this, apart from the belief of Taub, Miller, and Fowler (1949) that a superficial punctate keratitis (unconnected with onchocerciasis) can be attributed to allergy. On the other hand, it would seem that all the evidence points to such a lesion being typical of virus disease of the cornea. Trachoma, herpes febrilis, herpes zoster, molluscum contagiosum, even Newcastle disease, all virus infections, illustrate this point. Nevertheless, there is much to be said for the view that the punctate keratitis may occur as a result of a hypersensitive state. The widely scattered and fairly uniform distribution of the corneal opacities, so frequently described as due to onchocerciasis, is highly unlikely to have been caused by the death of parasites at each site. As a result of our work on experimental onchocerciasis, to be published later, such a large number of parasites as is postulated would almost certainly lead to a violent sclerosing keratitis. The very uniformity and equality of the distribution is against the claimed pathogenesis. How then may this reappearance of positive conjunctival biopsies with corneal opacities be explained other than by allergy?

The answer may lie in the coincidence of the periodicity of the virus keratides with the re-emergence of the parasites after Hetrazan therapy. It takes from 3 to 6 months for microfilariae to appear again in the skin after a course of 10 g. Hetrazan, and, as already noted, our cases of virus keratitis had either relapses or recrudescences roughly at the same interval. If the latter condition is treated with Hetrazan, some resolution would be expected, one might almost say despite the drug, and a flare-up 3 or 4 months later would not be surprising.

It has been shown elsewhere (Rodger, 1957) that the Individual Density Figure* in those suffering from onchocercal kerato-uveitis ranges between

* The Individual Density Figure is an index of the density of infection in the individual, marks being given for positive biopsies taken from the conjunctiva, neck, chest, thigh, and calf of both sides, repeated when negative.

26 and 31. Where corneal opacities were present along with pannus onchocercosus, the mean I.D.F. was 27; where such opacities were present in an otherwise healthy eye, however, the mean figure was 14 although the subject was suffering from onchocerciasis. With such a low figure it is difficult to accept onchocerciasis as the cause, except perhaps in the unlikely circumstance of a head-nodule being present.

IV. Histopathology of Punctate Corneal Opacities

The pathological findings on non-onchocercal punctate keratides reported in the literature are inconclusive and at variance. Duke-Elder (1937) quotes the mixed findings of Fuchs (1889), Nuel (1894), Verhoeff (1911), and Wright (1930). Samuels and Fuchs (1952) describe how a herpetic keratitis begins in the epithelium. It is partly attenuated, partly swollen, and in considerable disorder. The chromatin is dissociated and contracted in the centre, forming an intensely-staining eosin body, separated from the original membrane of the nucleus by an unstained zone. They call this a "herpes corpuscle". The nuclei of the basal epithelium cells no longer lie at right-angles to Bowman's membrane. The superficial layers of the stroma are in addition infiltrated by leucocytes. This histopathological picture was obtained by infecting the cornea of a single eye that had to be enucleated for carcinoma. Even here, however, the information is far from complete, since it describes the lesion at only one stage in its course.

Strong, Sandground, Bequaert, and Ochoa (1934) underline the poverty of information on the subject of onchocercal punctate keratitis; they reproduce photomicrographs and drawings from eleven cases where tissues were excised from the eye. In none of these, however, do corneal opacities appear. This is true also of the otherwise excellent photomicrographs of Hughes (1949). Hissette (1938) stated that he sometimes found in eye sections small nests of lymphocytes and monocytes, usually placed between the epithelium and Bowman's membrane. He could not conclude with certainty that they represented punctate opacities, although he was inclined to interpret them in that way.

Such scanty evidence shows that even less is known about the histopathology of onchocercal punctate opacities than about the punctate keratitis of virus origin. We obtained a little more evidence to add to this knowledge, which is given in detail below.

In the cornea of a patient suffering from acute onchocercal kerato-uveitis (I.D.F. 31), there were two corneal opacities (Figs 1 and 2, opposite) each about 1·0 mm. in diameter, one of the patch type and the other in the shape of a halo. They were situated on the outer margin of Bowman's zone. The segment of cornea was carefully excised without damaging the vital area. The opacities can be seen to form a depression in the epithelium through the thinning of that tissue, which is here only about 15 μ in width; both opacities are entirely superficial to Bowman's membrane, which seems to be undamaged. The basal cells of the epithelium are

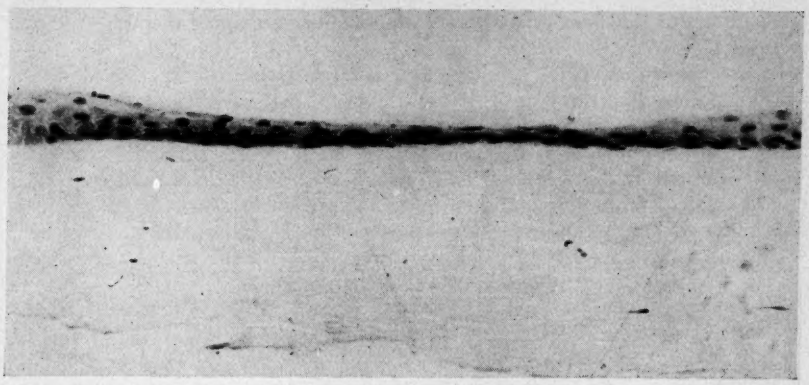

FIG. 1.—Corneal opacity in punctate keratitis of onchocerciasis. In this low-power view the full extent of the opacity can be seen. The epithelium alone is involved; it is depressed and atrophic; the nuclei are pyknotic; and the cells are flattened and in disorder. Haematoxylin and eosin. ×184.

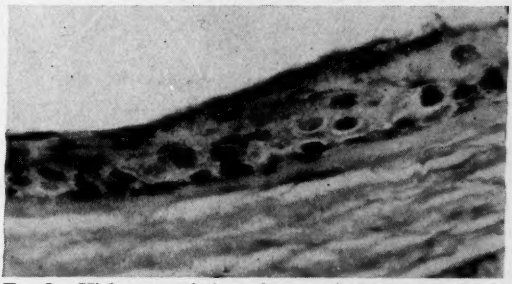

FIG. 2.—High-powered view of one end of same opacity as in Fig. 1 stained for mucin. Bowman's membrane is not affected. The mucoproteins of the basement membrane do not stain well. Nuclear pyknosis and disorder of the cells in the atrophic area can be seen. Periodic acid Schiff counterstained with haematoxylin. ×480.

disordered and flattened. The nuclei are pyknotic, and the nuclear alignment horizontal. The wing cells are similarly affected. Periodic acid Schiff does not stain the mucoproteins of the basement membrane. Pigment granules have invaded the epithelium at all levels, even outside the opacity in what looks like healthy epithelium. The underlying stroma is unaffected. This picture, restricted as it is to the epithelium, does not agree with those clinical descriptions of onchocercal punctate keratitis which state definitely that the stroma and not the epithelium is involved. If this is correct, then the present case cannot be one of punctate keratitis of onchocercal origin, and it may be submitted as evidence, therefore, that an old virus punctate keratitis exists here alongside an active onchocercal kerato-uveitis. In point of fact, as mentioned earlier, the outer margin of Bowman's zone is not an unusual situation for opacities of onchocercal origin. It may be recalled that the parasites are very commonly found lying between the

epithelium and Bowman's membrane, which would account for this histological picture.

In the second case, the appearance of the two opacities (Figs 3 and 4) was nearly identical with those in the first case, except that their size was slightly less and they lay on both sides of the second relucent line. The subject did not suffer and had never suffered from onchocerciasis. The ocular condition was quiet. The opacities lay below Bowman's membrane, which was unaffected. The epithelium had proliferated, and its nuclei stained darkly. The basement membrane was thicker than normal, was disordered and granular, and stained heavily with periodic acid Schiff. In the area of the opacity the fibroblasts in the stroma

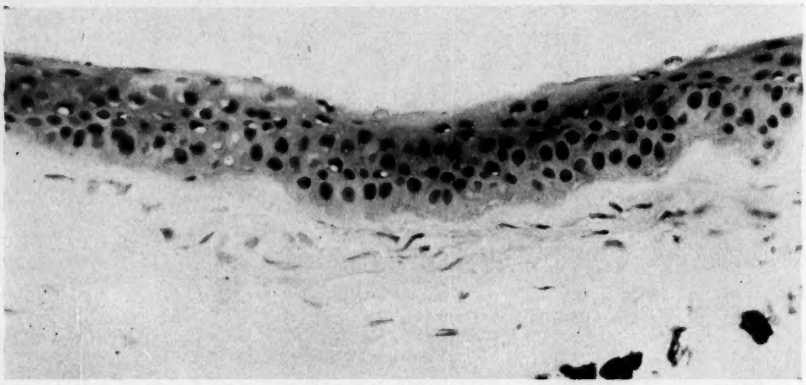

FIG. 3.—Corneal opacity in epidemic punctate keratitis. The epithelium has proliferated and its nuclei stain darkly. Bowman's membrane is irregular but otherwise unaffected. Below, in the stroma, there is an area where fibroblasts are more numerous than elsewhere. Haematoxylin and eosin. ×278.

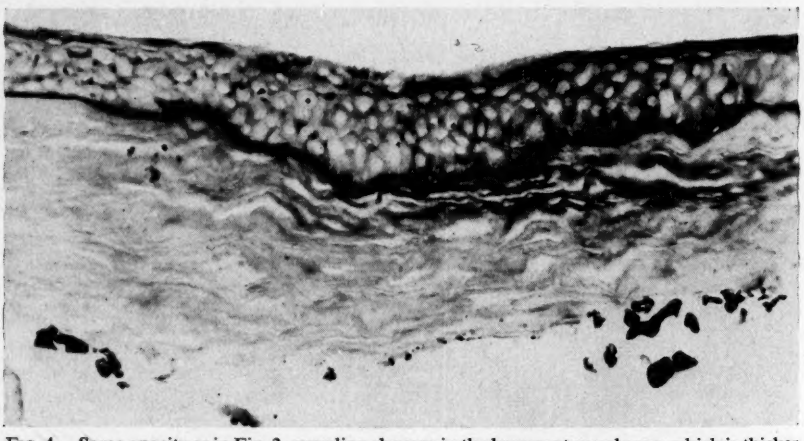

FIG. 4.—Same opacity as in Fig. 3, revealing changes in the basement membrane, which is thicker than normal and granular. The collagen fibres are disordered, and stain somewhat heavily. Periodic acid Schiff, not counterstained. ×278.

were more numerous than elsewhere. The collagen fibres were disorientated, and stained quite heavily with periodic acid Schiff. This case was diagnosed on clinical grounds as an old epidemic virus keratitis; the histological appearances are quite consistent with such a diagnosis.

Conclusions

It has been shown that the herpes febrilis and epidemic type of punctate keratitis are common in West Africa in non-endemic onchocerciasis areas, where there can be no doubt as to the diagnosis. Geographically, these areas are found next to endemic areas, so that there is no reason to suppose that the virus keratides are not also present in places where onchocerciasis exists; in fact, in patients within the endemic areas not suffering from the disease, virus keratides cases were equally common.

We believe that where the cornea is invaded by the microfilariae of onchocerca volvulus, the characteristic anterior lesions of ocular onchocerciasis will arise, and that in association with them there may appear superficial or interstitial punctate opacities of a type often slightly larger than those seen in the virus diseases and initially more dense, but in other respects similar. Where the anterior lesion is a limbitis, then complete resolution sometimes occurs, so that the end-result, a quiet eye with a few punctate opacities, may be similar to that found in the two other diseases.

Where a punctate keratitis is found to be active and severe, with many opacities scattered over the cornea but no sign of a characteristic onchocercal anterior lesion, two possibilities exist:

(1) the more likely in our view, the lesion is due to one or other of the virus keratides;

(2) there is a possibility that such a picture may occur as an allergic manifestation due to invasion of the cornea and the death of a few microfilariae (conjunctival invasion is not enough). There is no real evidence for this latter hypothesis, however. Invasion of the cornea by many microfilariae would almost certainly lead in the end to the death of several parasites, and a characteristic pannus onchocercosus would inevitably follow.

Summary

(1) The different types of punctate keratides found in the tropics are described, and the differences are stressed.

(2) The punctate keratides due to the herpes and epidemic-type viruses and those seen in onchocerciasis are shown to be somewhat similar. In a group of 750 African subjects, twenty-two, eleven, and eighteen cases of each disease respectively are described in detail. They were observed over periods of from 15 to 18 months.

(3) The aetiology of isolated punctate corneal opacities in a quiet eye is

discussed, and it is concluded that they are seldom due to onchocerciasis, even when the conjunctival biopsies are positive. In six cases, three will be due to the herpes virus, two to the epidemic type, and one to onchocerciasis.

(4) The histopathology of two cases is given, along with photomicrographs of the lesions.

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PRE- AND POST-OPERATIVE ACETAZOLEAMIDE (DIAMOX) IN GLAUCOMA SURGERY*

BY

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ACETAZOLEAMIDE (Diamox) has been used to lower temporarily the intra-ocular pressure in eyes with raised tension (Becker, 1954; Agarwal and Saxena, 1955), in restoring flat chambers after intra-ocular operations (Murphy, 1954; Thrope, 1955a; Agarwal, Sharma, and Malik, 1955), as a pre-operative measure in cataract surgery to diminish the incidence of complications, and to complete the operation without iridectomy (Agarwal and Malik, 1957). Thorpe (1955b) used the drug as a prophylactic measure in glaucoma surgery, starting 4 to 6 hours after operation in six cases, and showed that acetazoleamide seemed to assist the early restoration and maintenance of the anterior chamber. He also concluded, however, that the lowered intra-ocular pressure might lead to minimal cystic filtration bleb formation in the surgical drainage area, and might therefore contraindicate its use. He says that the series is rather small to draw any tentative conclusions. The purpose of this paper is to report on the use of acetazoleamide as a prophylactic, beginning at least 2 days before operation.

Material and Methods

Fifty cases of glaucoma admitted to the wards of the S.N. Hospital, Agra, were chosen for this study.

All patients were given on admission, besides the routine treatment for glaucoma, a single daily dose of 500 to 1,000 mg. acetazoleamide, depending upon the initial level of the intra-ocular pressure. The treatment was continued for 2 to 3 days. One hour before operation the patient was given a tablet of 250 mg. and a delayed-action capsule of 250 mg. acetazoleamide. This dosage was continued for a week after operation. The patient was subjected to a post-placed valvular iridencleisis.

Fifty other cases were used as controls and received no acetazoleamide until the fifth post-operative day. If the chamber had not formed by then, acetazoleamide 250 mg. was given daily.

Observations

Records were maintained of the initial ocular tension, the tension at the time of operation, and the tension at the time of discharge. The incidence of flat chamber and the nature of the drainage bleb were also noted (Tables I to III, overleaf). Particularly in cases with high intra-ocular pressure, the administration of acetazoleamide lowered the tension and diminished the congestion, so enabling the surgeon to carry out the operative procedures with greater ease.

* Received for publication January 29, 1957.

TABLE I
OCULAR TENSION IN PATIENTS AND CONTROLS

Tension (mm. Hg)	At Admission		At Operation		At Discharge	
	No Diamox	Diamox	Controls	Series	Controls	Series
Below 25	nil	nil	nil	nil	36	40
25 to 30	4	3	6	25	10	8
31 to 40	6	6	10	15	4	2
41 to 50	14	13	15	8	nil	nil
51 to 60	20	13	15	2	nil	nil
Over 60	6	15	4	nil	nil	nil

TABLE II
INCIDENCE OF FLAT CHAMBER

Cases	Number Treated	Flat Chamber (days)					Per cent. Fifth Day
		1	2	3	5	7	
No Diamox	50	30	25	25	21*	4†	42
Diamox	50	12	5	4	3*	2†	6

* Diamox given on this day. † Air injected on this day.

TABLE III
ADEQUACY OF DRAINAGE

Cases	Number Treated	Drainage	
		Adequate	Inadequate
No Diamox	50	40	10
Diamox	50	38	12

The incidence of flat chamber was considerably reduced (from 42 to 6 per cent.). The drainage bleb formed, though less cystic than in control cases, was adequate, and the drainage of aqueous humour was satisfactory.

Discussion

Acetazoleamide produces a certain degree of hypotension in glaucomatous eyes by the inhibition of the secretion of aqueous humour. Its pre-operative use assists glaucoma surgery. We have always felt that there is some risk in operating upon eyes with very high ocular tension. A valvular iridencleisis in itself obviates some of the dangers due to gradual decompression of the eyeball, and pre-operative acetazoleamide reduces these dangers still further. Mulberger and McDonald (1956) state that the pre-operative lowering of the intra-ocular pressure by miotics or other means makes operative procedures more difficult, but we have found the lowering of the intra-ocular pressure to near the normal level conducive to better results.

We have already reported on the efficacy of this drug in the restoration of the anterior chamber after glaucoma surgery (Agarwal, Sharma, and Malik, 1955).

The incidence of flat chamber up to the fifth post-operative day in the control series of cases (42 per cent.) and in the cases in which acetazoleamide was given (6 per cent.) speaks for itself. Thorpe (1955a) suggested that the prophylactic use of this drug assisted early restoration and maintenance of the anterior chamber, but he did not rule out the possibility of spontaneous restoration. The present series indicates that the restoration of the anterior chamber is a definite result of pre- and post-operative acetazoleamide administration.

Thorpe (1955b) raised a doubt about the advisability of using the drug pre-operatively because of the risk of minimal cystic bleb formation and inadequate drainage. We followed up the results of iridencleisis in our test cases, and found that the bleb formed was not as cystic as in the control series, but the adequacy of drainage was never in doubt and the percentage of successes equalled that in the cases in which no acetazoleamide was given. It is said that iridencleisis is not a safe procedure in cases of glaucoma with high ocular tension, but post-placed valvular iridencleisis with early massage of the globe has been suggested (Agarwal, 1957) in such cases, and the use of acetazoleamide before and after the operation is of further assistance.

Summary

(1) Fifty cases of iridencleisis in which acetazoleamide was administered pre- and post-operatively form the basis of this study.

(2) The efficacy of this drug in the restoration of flat anterior chambers after glaucoma operations is confirmed, and its use in the prevention of flat chamber is suggested.

(3) Its pre-operative use in reducing intra-ocular pressure to facilitate iridencleisis, especially in patients with high ocular tension, is suggested.

(4) The fear of its adverse effect on drainage after glaucoma operations is discounted.

(5) Its routine use before and after glaucoma surgery is suggested.

We are grateful to Lederle Laboratories, Pearl River, New York, for the supply of Diamox (acetazoleamide).

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Brit. J. Ophthal. (1957) **41**, 616.

PLASTIC REPAIR OF CONJUNCTIVA WITH PERITONEUM TRANSPLANTATION*

BY

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THE repair of conjunctival defects has always been a difficult problem. From time to time various tissues, such as Thiersch's graft, mucous membrane from the oral cavity (lower lip and cheeks), inferior turbinates of the nose, amniotic membrane, and even skin from the prepuce and labia minora have been utilized. Mucous membrane from the oral cavity is most commonly used for grafting into the conjunctival sac. However, it is difficult to obtain the required extent of mucous membrane from the oral cavity, and, when such a graft takes, it tends to stand out thick and prominent and to differ in colour from the rest of the conjunctiva, so that the cosmetic results are generally unsatisfactory.

In 1954, while working in the general surgical department at Hexham Hospital, Northumberland, England, I was struck with the extreme thinness and transparency of the inguinal hernial sac and with its suitability for transplantation into the conjunctival sac. It was not until late 1956 that I was able to undertake an experimental study of this problem. To date, I have successfully transplanted slips of peritoneum on to palpebral conjunctiva in 23 cases of entropion (modified Webster's operation), and on to bulbar conjunctiva in two other cases. In another case, the whole of the mucous membrane of the contracted socket was dissected out and replaced with peritoneum. The results of these trials are described below.

Case Reports

Case 1, a man aged 45 years, attended the ophthalmic out-patient department of the Willingdon Hospital on September 3, 1956, complaining of watering and irritation in both eyes for a long time.

Examination.—He had advanced trachoma with entropion in both eyes. As an experimental measure the right eye was selected for a modified Webster's entropion operation with peritoneal graft.

Operation.—On September 6, 1956, under local anaesthesia, the upper eye-lid was everted on the straight edge of a divided spatula,† and fixed by three dark silk sutures passed through the lid margin. The silk sutures were pushed into the vertical slits and stretched, so that the lid was maintained in the everted position. A linear incision was made in the sulcus subtarsalis, exposing the orbicularis oculi muscle which should not

* Received for publication February 22, 1957.

† As no Webster spatula was available, a substitute was devised. A wooden tongue spatula was divided into two equal lengths by cutting it down the middle. At the rounded end of one half, three linear slits were made with a razor blade or with a metal file (such as is used for cutting ampoules). These cuts extended through less than a quarter of the length as shown in Fig. 1 (opposite).

FIG. 1. — Webster spatula devised from a wooden tongue depressor.

be cut. The edges of the tarsus including the two ends, were undermined all round. A rectangular piece of thin peritoneum larger than the size of the incision was cut and placed *in situ* in this prepared bed.

The length of the raw area of the sulcus subtarsalis should be measured with calipers. Much time is saved if the peritoneum is kept stretched by the assistant and a loop is made with a double-armed suture on the smooth side at each end of the intended slip (Fig. 2).

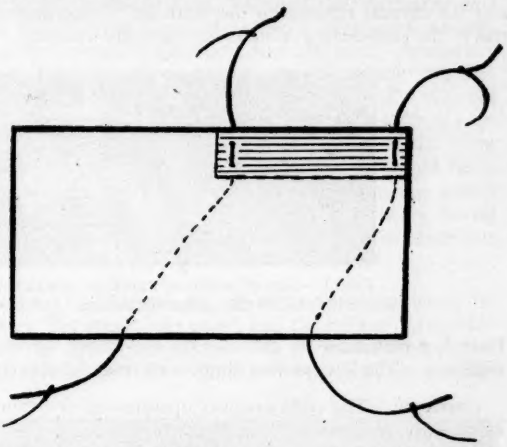

FIG. 2.—Piece of peritoneum stretched by assistant. Slip of peritoneum to be cut is shown by shaded area. Loop of mattress suture is on the side of the peritoneum which is lined with mucous membrane.

The peritoneum is cut with scissors, care being taken not to cut the sutures, and is transferred to the prepared undermined bed, the edges being eased under the edges of the tarsus incision. The two needles at each end are then passed through the thickness of the lid, from beneath the undermined ends of the incision in the sulcus subtarsalis, so as to emerge on to the skin side where the threads are tied. Penicillin eye ointment was applied and the eye bandaged. Bandage and stitches were removed on the fifth day.

Result.—The graft was found to have taken firmly and well, and the entropion was completely relieved with a satisfactory cosmetic effect. The case has been followed for 2 months and the result is quite satisfactory.

The modified Webster operation with peritoneum graft (as described for Case 1) has now become the routine practice for the treatment of entropion in the Willingdon Hospital, and the same technique has been used in 22 similar cases with excellent results.

Case 2, a man aged 56, attended complaining of recurrent pain in the left eye for 6 months.

Examination.—There were degenerative corneal opacities, hypermature cataract,

chronic iridocyclitis, and secondary glaucoma. There was no perception of light. The patient readily agreed to enucleation, but it was decided to retain the eye for experimental purposes and to replace a slip of bulbar conjunctiva with peritoneum.

Operation.—In addition to instillation of local anaesthetic, a retrobulbar injection of Novocain and adrenaline was also given to lower the ocular tension. The superior bulbar conjunctiva was incised in a curve 2 mm. from and concentric with the limbus, and a slip of conjunctiva about 2 cm. long and 0·5 cm. wide was dissected away, removed, and replaced with a peritoneum graft of the same size which was stitched in position. After the peritoneum graft was stitched, a limbal incision was made and a broad iridectomy was done at 10 to 2 o'clock; 20 minutes later, the incision was enlarged with corneal scissors and the calcareous lens was removed with a wire vectis. Side-to-side corneoscleral stitches were applied, atropine 1 per cent. drops and penicillin ointment were put in, and the eye was bandaged.

Result.—Post-operatively the patient was very grateful at having been relieved of the severe pain. When the bandage was opened on the fifth day, the graft was well in position (Fig. 3). The conjunctivo-peritoneal stitches were removed on the seventh day and the corneal stitches on the tenth day. The graft was white as compared with the rest of the conjunctiva, which was markedly inflamed. The case is still being followed.

FIG. 3.—Slip of peritoneal graft in position lying concentric with the limbus, 20 days after operation. Left eye rotated downwards.

Case 3, a man aged 56, attended on November 7, 1956, for a cataract operation in the right eye. The left eye was blind, with total corneal opacity and convergent squint.

Operation.—The right eye was operated on for cataract on November 15, 1956, and at the same session the whole of the bulbar conjunctiva in the left eye, up to the superior lateral and inferior fornix, except the medial part, was replaced with a peritoneum graft. The peritoneum used in this case had been stored in an ordinary refrigerator at 4° C.

Result.—The bandage was opened after 5 days, and it was found that the graft had taken well, except in the inferior part where it had been dislodged by a haematoma and rubbing of the graft by the lower lid. The colour was changing and merging with the rest of the conjunctiva (Figs 4 and 5).

FIG. 4.—Left eye before operation.

FIG. 5.—After peritoneum has been grafted into the superior and lateral part of the inferior bulbar conjunctiva.

Case 4, a man aged 60, attended the out-patient department on November 30, 1956, with cataract in the right eye. The left socket was contracted. The right eye was operated on for cataract on December 6, 1956, and, as the patient was very glad to regain his vision, he was coaxed into agreeing to an experimental operation on the contracted left socket.

Operation.—On December 20, 1956, the conjunctiva of the whole of the contracted socket was removed, and the socket was deepened to the required size, particular care being taken to deepen the inferior fornix. The fibrous scar tissue underlying the conjunctiva was also dissected away, and complete haemostasis was obtained. A negative mould of the prepared and enlarged cavity was made with dental casting material. Peritoneum (which had been stored for 18 days in the refrigerator at 4° C.) was cut roughly to the required size and shape of the raw area of the socket. The inferior edge of the prepared piece of peritoneum was stitched to the conjunctival edge of the lower lid, taking care that the raw surface of the peritoneum when in position would lie in contact with the raw surface of the socket. Now this piece of peritoneum was placed on the mould, the cavity was sprinkled with crystalline penicillin powder, and the mould was placed in position into the socket. No lid stitches were applied. A bandage was applied firmly and procaine penicillin injections were given for 4 days.

Result.—The bandage was opened on the eleventh day after the operation, when the mould was removed from the cavity. The socket was clean, and the inferior fornix was deep and the socket as large as on the day of operation. The peritoneo-conjunctival stitches were removed, and the peritoneal graft was found to be perfectly in position (Figs 6, 7, and 8, overleaf).

FIG. 6.—Left contracted socket before operation.

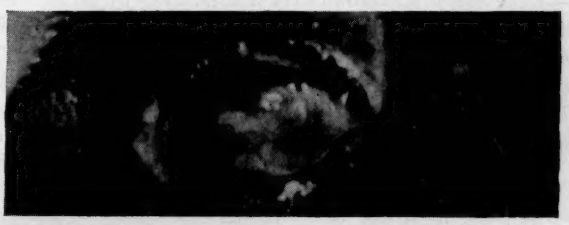

FIG. 7.—Socket 36 days after grafting operation.

FIG. 8. — View from above to show the line of junction. The inferior fornix is as deep as in any normal case.

Discussion

Peritoneum from hernial sacs and tunica vaginalis from hydrocoele sacs are readily available in large amounts, and can be stored for up to 18 days in normal saline at 4° C.

In attempting to graft peritoneum, great care is needed to see that the endothelial surface of the peritoneum is kept flush with the rest of the conjunctiva. The raw surface of the peritoneum is easily identified as it has a fibrous appearance and is rough to the touch. If the very thin portion of the hernial sac is not available, the fibrous tissue should be peeled off from the mucous lining of the peritoneum so as to secure a graft as thin as the conjunctiva.

Suggested Indications in Ophthalmology

I. Trauma

(*i*) *Repair of Contracted Socket.*—The whole of the socket can be repaired at one session as was done in Case 4. The advantages as compared with Thiersch's graft are very obvious, because there is no discharge, irritation, or sodden appearance. The cavity is always clean, as is any cavity lined with mucous membrane, and the colour is rather similar to the normal appearance of the conjunctiva.

(*ii*) *Repair of Bulbar Conjunctiva.*—This may be necessary after removal of tumours, contractures, fixation of the globe after pterygium operations, removal of dermolipoma, all kinds of burns, and other extensive injuries. The sclera shines through the transparent peritoneum and therefore matches closely the rest of the conjunctiva.

(*iii*) *Recurrent Pterygium.*—After having dissected the head of the pterygium off the cornea and cut it away, a small slip of peritoneum may be placed along the edge of the cornea. This procedure is now being studied.

(*iv*) *Symblepharon of any Origin*

II. Inflammation

(*i*) *Trachoma*

(*a*) In the sequelae of trachoma—particularly entropion, symblepharon, and pannus.

(*b*) It is suggested that the course of trachoma may be arrested by replacing the affected conjunctival surface with peritoneum. In the treatment of pannus, a slip of peritoneum may be stitched in position after doing a partial or total peritomy.

(ii) *Essential Shrinkage of Conjunctiva*

(iii) *Other Vesicular Conditions*

III. Neoplasm

To replace the conjunctiva when this tissue has to be sacrificed during the treatment of new growths, by operation or radiology. I have seen fixation of globe even after the removal of a dermolipoma, when no portion of the conjunctiva was removed.

IV. Degenerations and deficiency and metabolic disorders of the conjunctiva

Xerosis and acne rosacea

V. Operations

To act as a support in various surgical operations on the cornea and iris such as keratoplasty and iris prolapse.

Summary

(1) The results of transplantation of peritoneum on to the conjunctiva to fill gaps in the conjunctival sac are described in four cases. Excellent results were achieved in 23 cases of entropion, and this method is now used as routine in the surgical treatment of entropion in the Willingdon Hospital, New Delhi.

(2) On the basis of the successful results obtained, it is suggested that replacement of conjunctiva by peritoneum may be undertaken in trachoma and other inflammatory diseases of the conjunctiva and after surgical removal of the conjunctiva in the treatment of neoplasms.

(3) This new transplantation material is particularly useful for socket reformation, lid repair, or new lid formation, and for repair of the bulbar conjunctiva.

(4) Because of the similarity of peritoneum and conjunctiva in thinness, colour, and transparency, the cosmetic results have been encouraging. It is not yet possible to say whether in the long run the transplanted peritoneum will merge imperceptibly with the surrounding normal conjunctiva. Cases are being followed-up over a long period in order to study this point.

(5) A further study of the pathological, bacteriological, and other aspects of this transplantation technique is now being made.

I wish to express my gratitude to Col. B. K. Shorey and my other surgical colleagues in the hospital for providing me with samples of peritoneum. I am particularly indebted to Surgeon-Capt. B. L. Taneja for his interest in this work. My thanks are due to Dr. N. C. Singhal for his helpful suggestions.

Brit. J. Ophthal. (1957) **41**, 622.

APPLIANCES

THE FIXATOR*

BY

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THE apparatus described here has been designed to afford an accurate test of binocular fixation, and to allow a comparison of visual acuities in the two eyes at reading distance.

Fig. 1 illustrates the principle of the fixator. The two pictures are represented diagrammatically by two arrows. In front of the pictures is a pair of 20 D biconvex lenses, and each of these lenses forms an inverted image of one of the pictures. The two inverted images are made to coincide on the plano face of a plano-convex lens placed 33 cm. in front of the observer. This lens does not appreciably alter the position of the images.

It will be observed that each eye sees only the image of the picture of the opposite side. The two pictures may be the same, with control marks added. Three of the clues which normally enable the position of an object in space to be perceived operate here to locate the images on the surface of the lens; these are the stereoscopic clue of binocular parallax, the parallax due to head movements, and the vergence of the light.

Function of the Plano-Convex Lens

This is of such a strength, 13 D, that it forms images of the biconvex lenses in the pupils of the observer so that these lenses cannot be seen. If the plano-convex lens is removed from the apparatus, the position of the superimposed images is scarcely affected, but now however the two biconvex lenses and their surrounds are clearly visible behind the images; and, since the images do not obstruct the view of anything behind them, there is a strong psychological stimulus to think that the images are in or behind the biconvex lenses. With the plano-convex lens in position, nothing behind it is visible, and the two superimposed images lying in its plano surface are perceived in their correct position.

A second function of the plano convex lens is to reduce distortion. Fig. 1 (opposite) shows that only that portion of the biconvex lens which is imaged on the pupil is in use at any one moment. For a pupil diameter of 4 mm. this will be $\frac{10}{33}=4\times1{\cdot}3$ mm. The head, however, is free to move anywhere, provided that the eyes remain in the images of the biconvex lens. These meet in the mid line, and so have a diameter of 65 mm. From this it follows that no adjustment for inter-pupillary distance is required.

* Received for publication April 4, 1957.

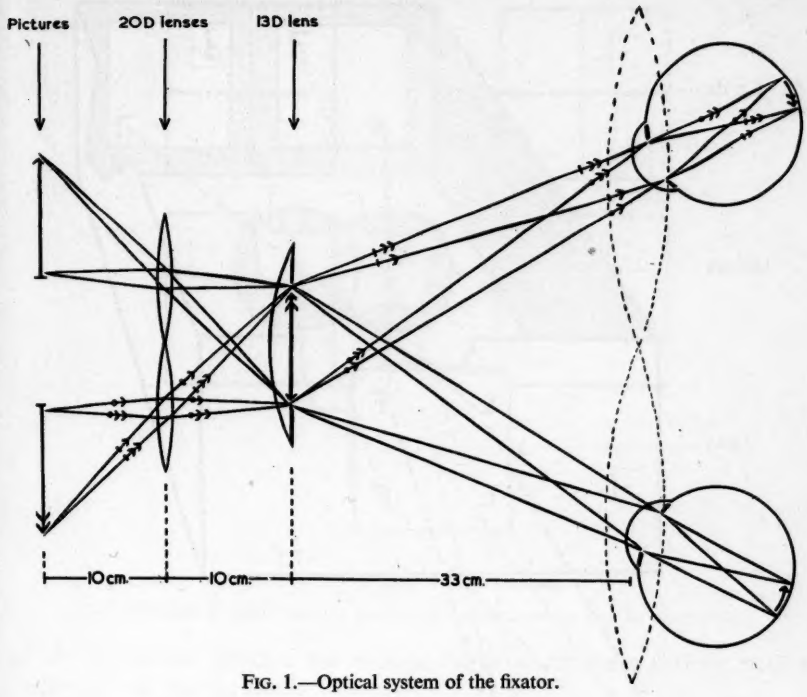

FIG. 1.—Optical system of the fixator.

Errors of Fixation

Fig. 2 (overleaf) shows a perspective drawing, in which the path of the central ray from each of the letters of the two pairs is shown by a dotted line. Square lenses are used. The two visual axes are shown by continuous lines accurately converged upon a mark on the front face of the plano-convex lens.

Consider the pair of letters LF, the images of which are formed in the upper part of the front lens. The F is on the right and is seen by the right eye; the L is on the left and is seen by the left eye. Suppose now that the eyes diverge from correct fixation; the visual axis of each eye will come nearer to the letter seen by that eye, and the result will be that the two letters will appear to the subject to approach each other. However, the opposite is the case for the bottom pair of letters, for here each eye sees only the letter of the opposite side, so that when the eyes diverge each directs its visual axis further away from the letter perceived by it, with the result that the letters appear to separate. Thus the position of the letters as reported by the patient indicates the direction of any error of fixation. The principle of this test is the same as that of the T.I.B. double mirror test.

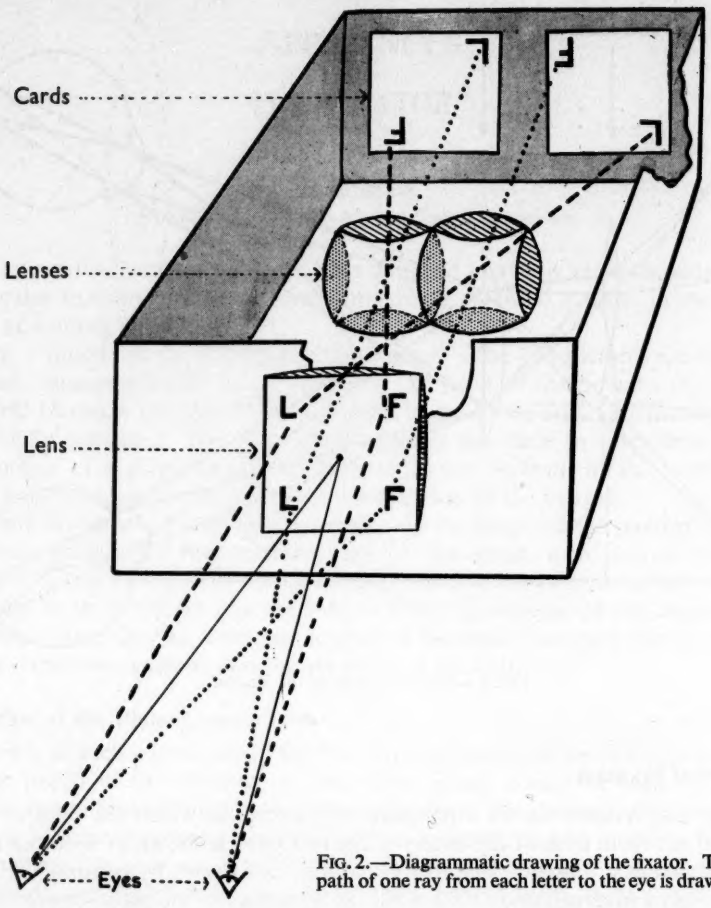

FIG. 2.—Diagrammatic drawing of the fixator. The path of one ray from each letter to the eye is drawn.

Nature of the Test

It must be emphasized that this apparatus does not measure latent squints. In a latent squint measurement there is nothing common to the view of the two eyes; in this apparatus, the common element in the two fields which provides a fusion stimulus, is under the control of the operator. Fig. 3 (*a*)–(*c*) shows three cards. In (*a*) the central lines afford a fusion stimulus, in (*b*) the square frame-work to the letters supplies a weaker peripheral stimulus, and in (*c*) the only stimulus to fusion is that provided by the edge of the lens and the outline of the front of the apparatus. An alternative to using a central fusion stimulus on the cards is to make a mark on the face of the front lens to act as fixation point. Alternatively, any small object such as a pin may be held on the surface of the front lens to act as a fixation target. The position

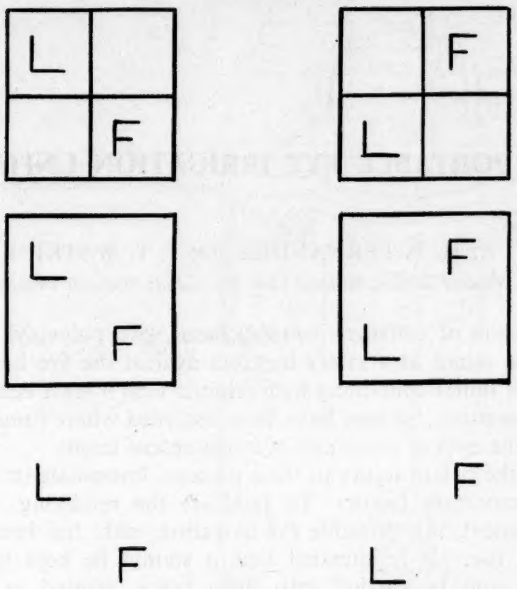

FIG. 3.—Cards to show how the amount of fusion stimulus may be controlled.

of the letters will indicate the accuracy with which these entirely natural fusion stimuli may be fixed.

Preliminary results show that, as would be expected, the nature of the fusion stimulus has a considerable effect on the accuracy of binocular fixation.

Use of the Instrument

It is possible that the symptoms of eyestrain, which frequently occur in cases of latent squint, may be due, not directly to the latent squint itself, but to errors of fixation induced by it; this instrument will afford a method of detecting such errors.

After operation and or orthoptic treatment for squint, it is hoped that the instrument may supply a more accurate indication of binocular function than is afforded by the cover test or the stereoscope.

After full correction for distant vision has been given, comparison of visual acuities at the reading distance will reveal the rare condition of unequal accommodation in the two eyes.

My thanks are due to Mr. A. E. Turville for stimulating me to design this instrument, and to Mr. Jameson Evans, Dr. R. H. Bolton, Miss I. M. Whitney, Miss M. E. Wesson, and Miss H. Kilmister for preliminary trials with the instrument and for many helpful suggestions.

It is hoped that Messrs. Newbold and Co., Ltd., 46 Osnaburgh St, N.W.1., will shortly be able to supply this instrument.

Brit. J. Ophthal. (1957) **41**, 626.

PORTABLE EYE IRRIGATION UNIT*

BY

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THE introduction of conveyor belts surfaced with polyvinyl chloride compounds in the mines as a safety measure against the fire hazard may give rise to irritant fumes containing hydrochloric acid if such belting is exposed to high temperatures. Cases have been recorded where fumes have caused irritation to the eyes of personnel of mines rescue teams.

To reduce the risk of injury to these persons, immediate irrigation of their eyes is an important factor. To facilitate the rendering of appropriate first-aid treatment, this portable eye irrigation outfit has been designed for underground use. It is intended that it should be kept with the mines rescue team, and be carried with them below ground as part of their emergency first-aid equipment. The irrigation unit can also form part of the normal medical treatment centre equipment for use for eye irrigation, irrespective of the cause.

CONSTRUCTION

The irrigation outfit is housed in a wooden box $12\frac{3}{4}'' \times 6\frac{3}{4}'' \times 5\frac{1}{4}''$. It has a hinged door, allowing free access to the equipment. This door is kept secure by two small clamps when the unit is not in use. At the top of the box is a carrying handle.

Normal saline solution is used for irrigation. This is retained in a Dextraven bottle, which consists of a glass bottle (B) with a rubber bung and screwed cap. The bottle is retained in the upside-down position in the wooden box by a wooden clamp (C), screwed in position as shown in Fig. 1. (opposite). Air is allowed to enter the bottle through a long, piercing 8" intravenous needle (N), which pierces the rubber bung of the Dextraven bottle. The needle is connected by a length of 3-mm. bore rubber tubing (R1) with walls 1-mm. thick to a glass eye-dropper tube (E1), which contains a plug of cotton wool (W) to act as a filter. The tapering end of this glass tube facilitates connexion with the rubber tube. The glass tube and part of the rubber tube are held by two small Terry clips (T1 and T2). Fluid runs out of the bottle through a small glass tube (G) piercing the rubber bung and connected with a further length of tubing (R2) of 3-mm. bore and 1 mm. thick. This is threaded through a Mohr's clamp (M) as shown in Fig. 1. Another eye-dropper tube (E2) is fixed at the end, but this time with the tapering end outwards.

* Received for publication April 4, 1957.

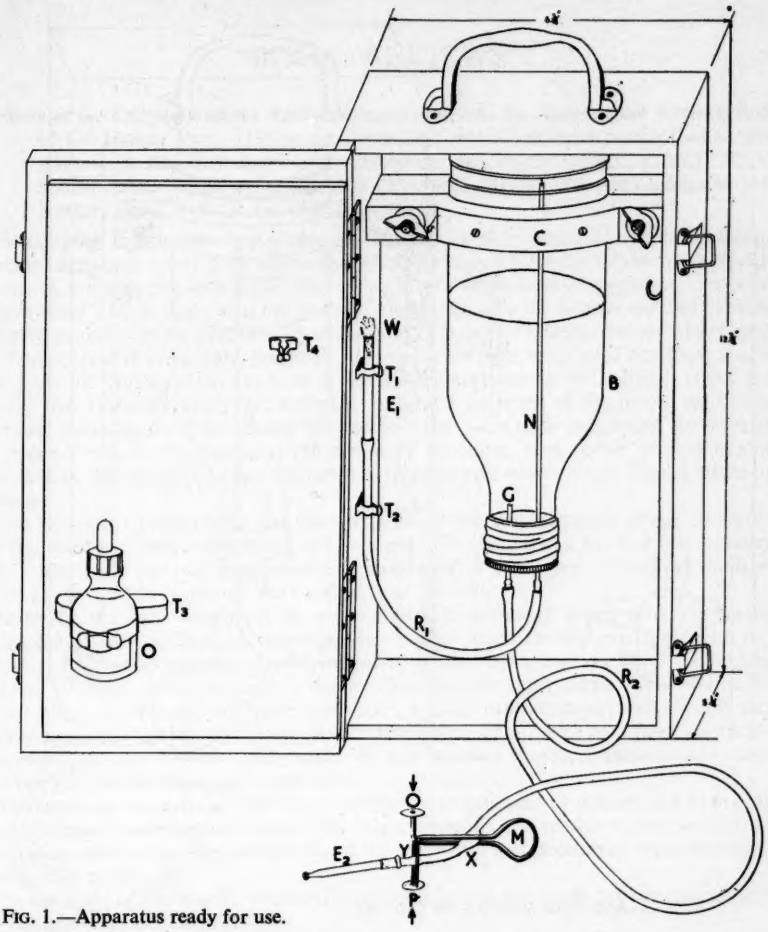

FIG. 1.—Apparatus ready for use.

The threading of the tube through the clamp in the manner indicated in Fig. 1 allows the dropper to be held in the clamp with finger and thumb at O and P, the other hand being free to hold open the eyelids. In the position shown, the clamp prevents any fluid running out of the bottle as the tube R2 is nipped at X. If the clamp is pressed firmly together at O and P, the rubber tube is again nipped at Y and again the fluid will not run. Only when the clamp is pressed gently will fluid come through. This prevents a clumsy person from squirting fluid all over the face, as irrigation only takes place when gentle pressure is applied.

On the door of the box is a large Terry clip (T3) housing a bottle of Ocusol eye-drops (O).

When the box is being carried, the fluid may have a tendency to jerk through

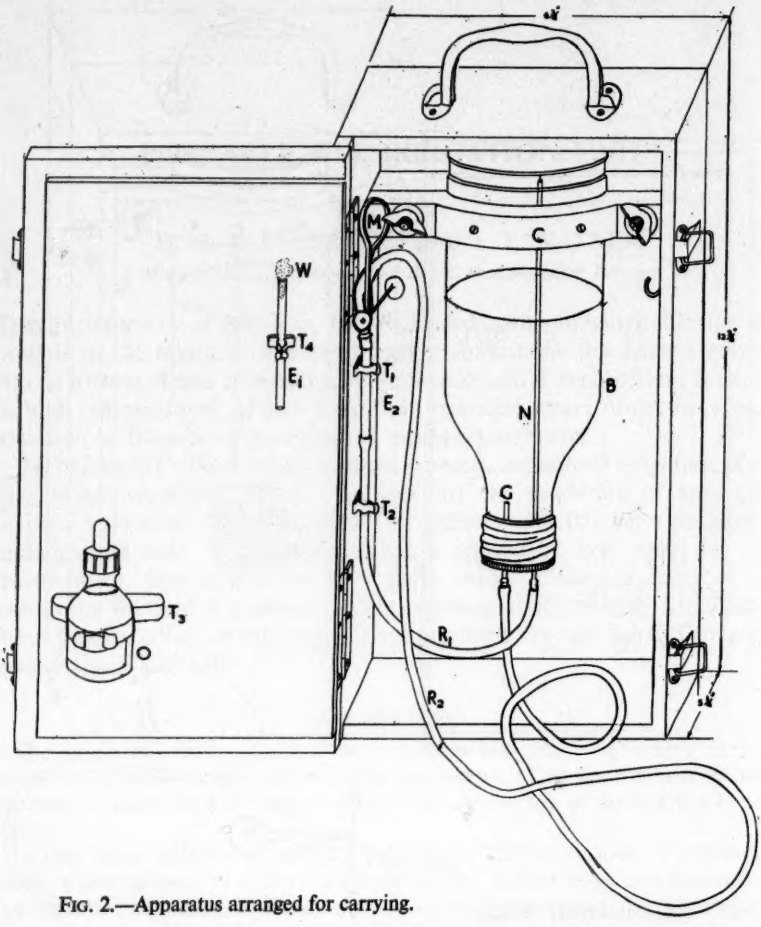

FIG. 2.—Apparatus arranged for carrying.

the air inlet, and to moisten the cotton wool. If the wool is wet it will prevent air flowing through; to avoid this the glass tube (E1) containing the cotton wool is removed and placed in the small Terry clip (T4) on the door (Fig. 2). The tip of the second glass eye-dropper (E2) is then inserted into the rubber air inlet tube (R1) as shown in Fig. 2.

The box is strongly made, and the apparatus is simple and stout. It has been found that rough handling does not interfere with its efficiency.

We are grateful to Mr. A. J. G. Coulshed, M.Sc., M.I.Min.E., East Midlands Divisional Rescue Station Manager, for his assistance in constructing the apparatus, and to Mr. W. Morley, of the Survey Department, No. 4 Area, East Midlands Division, National Coal Board, who drew the diagrams.

Brit. J. Ophthal. (1957) **41**, 629.

BOOK REVIEWS

A Study of the Entry of Various Antibiotic Substances into the Aqueous and Vitreous Body of the Human Eye. (Untersuchungen über das Eindringen antibiotischer Substanzen in Kammerwasser und Glaskörper des menschlichen Auges.) By G. Saubermann. 1956. *Ophthalmologica* (*Basel*), Suppl. 46. Pp. 108, 93 refs. Karger, Basel. (*Swiss Frs* 13.50).

While much information is available concerning the effectiveness of antibiotics against various organisms, there is an undoubted need for more knowledge of the most efficient means of bringing the antibiotics into contact with the infecting organism. Professor Saubermann's book deals with the entry of antibiotics into the human eye and provides valuable guidance in the treatment of corneal and intra-ocular infections since his approach to the problem is essentially practical. Human eyes only were used for these studies and since the opportunities for such investigations are necessarily limited it is not surprising that relatively little information is presented for some of the newer antibiotics. The eyes available for these studies were those which were to be enucleated for a variety of reasons, but, in the majority, inflammatory processes were active or had become quiescent so that conditions approximated to those in eyes which would require antibiotic therapy.

The laboratory methods for the determination of the concentration of the antibiotics are described in considerable detail, and, while this is essential in a work of this standard, it is unfortunate that the cumbersome presentation of examples of these methods on pages 13–22 tends to interrupt the continuity of the text.

However, the experimental results are presented in a manner which is interesting and which reflects the painstaking nature of this study. Each antibiotic is dealt with in a separate section and the results are preceded by a short but useful review of the findings of other workers, much of which is derived from animal experiments. The limitations of the latter are evident with some antibiotics, *e.g.* chlortetracycline (aureomycin), oxytetracycline (terramycin), and tetracycline; experiments on animals with these substances suggested that they did not easily enter the eye whereas Professor Saubermann shows that entry is possible into the human eye.

The condition of each eye used in an experiment is indicated by a brief clinical history. This is a most useful feature since, with this knowledge, the reader is able to form his own opinion as to how far penetration of the antibiotic was dependent upon the pathological state of the eye.

On the basis of the results, practical recommendations are made for the treatment of corneal and intra-ocular infections.

A particularly valuable feature of this book is that, at the end of each section, the information obtained and the suggested usage of each antibiotic is summarized so that quick reference to the essential findings is simplified.

The Eye in Diabetes Mellitus. (L'occhio nel diabete mellito.) By G. Alagna and F. Scullica. 1956. Pp. 190, 89 figs (5 col.). G. D'Anna, Messina-Firenza.

This is a remarkably interesting and complete account of the many ocular complications which occur in diabetes as they affect the cornea, the iris, the lens, the refractive condition, the ocular tension, the oculomotor apparatus, the optic nerve, and—particularly in great detail—the retina. It is well and critically written, giving an excellent general survey of the clinical problems involved without going into vast detail. The illustrations are numerous and unusually good. Altogether it is a most satisfying publication, beautifully produced.

Optics, the Science of Vision. By V. Ronchi, trans. E. Rosen. 1957. Pp. 360, 128 figs. New York University Press. *($10).*

Italy, for all her grandeur, has not produced more than a handful of visual scientists. It is therefore interesting to welcome to the bookshelf the arrival of Ronchi's "Optics". The author, a distinguished physicist, famous for his diffraction test, sets himself a task worthy of a scientist and a philosopher. It is useless, he argues, to consider optical apparatus in the abstract. The strength of a chain is determined by the weakest link: hence the limitations of the visual apparatus must be considered when those of instruments are under discussion. This survey, however, which takes the reader from geometrical optics to electrophysiology and on to wave-theory, has many defects. The account of the accommodation of the eye, for example, accompanied by a figure with a lens of which the anterior surface has a smaller radius of curvature than the posterior surface, is flimsy in the extreme. Again, when the author discusses the duplicity theory of nervous messages, his treatment of the subject lacks experimental support. The author speculates and sometimes admits this. The choice of his subject matter is his responsibility; but he makes no case for including standard wave-theory, dealt with more comprehensively in other books, and for omitting any mention of the Stiles-Crawford effect, which one would have thought to be fundamental to visual optics. Of 128 figures only two represent graphs of experimental results and neither has any bearing on the subject. There are no references (they would occupy an "interminable list", and therefore the author has "dispensed with the compilation of such a list"). The style, partly due, one surmises, to the translator, an American professor of history, is quaint. Mental images are called "effigies"; "the human visual apparatus consists of two balls, contained in sockets alongside the nose"; "but we need not resort to binocular vision in order to land in this sort of quandary"—these are among the choicer examples. The publishers have lavished much affection on the production of this volume, but one cannot help feeling that $10 is too high a price to pay for a book of this sort.

Comparative Anatomy of the Eye. By J. H. Prince. 1956. Pp. 418, 151 figs, 62 refs. Thomas, Springfield, Ill. (63*s.*).

Prince's "Comparative Anatomy of the Eye" is in a sense a companion volume to his "Visual Development" which appeared in 1949. In its essentials the book is a survey of the anatomy of the orbit and of the eye in Vertebrates. A short section of 31 pages is devoted to the main features of the eyes of representative Invertebrates.

In considering the vertebrate eye, each tissue is taken *seriatim* and its main variations within the vertebrate phylum are discussed. Only essentials are dealt with and much of the minutiae omitted, probably a sound policy since the book is written principally for "medical men, optometrists, and veterinarians". There is no doubt that a book of this type is required in the literature.

One of the curiosities of the book is the use of italics in classifying animals: thus we read, on p. 201, of the "*frog hyperolius*", or the "*tree snake driophis*", where most people would expect the "frog, *Hyperolius*", and the "tree snake, *Dryophis*". Again, *carnivores*, on p. 205, is taken to mean carnivorous marsupials; and so on. There are also one or two contradictions which will doubtless be corrected in a subsequent edition. On the whole the book forms interesting reading in a subject which is not sufficiently appreciated by the average ophthalmologist.

***Gifford's Text-book* of Ophthalmology,** 6th edition. By F. H. Adler. 1957. Pp. 499, 277 figs, 26 col. pl. Saunders, Philadelphia. (£2 12*s.* 6*d.*).

The sixth edition of Gifford's "Ophthalmology" has now appeared under the editorship of F. H. Adler of Baltimore. This is a well-known and deservedly popular book in America for the student and general practitioner, and covers the whole field of

ophthalmology including related general diseases and diseases of the nervous system. It confines itself to the more common and important conditions and wisely avoids burdening the reader with clinical rarities. The section on ophthalmic surgery is short and confines itself to the more common surgical procedures. A welcome feature in this edition is the fact that injuries of the various tissues are collected together into a useful separate chapter.

On the whole the book serves its purpose admirably and exception can be taken to relatively few points. Virus diseases, for example, which are assuming greater importance every year, are hardly adequately discussed. Epidemic kerato-conjunctivitis, although stated to be "apparently caused by a virus", is put under the heading of "allergic conjunctivitis"; nor are virus diseases of the uveal tract adequately stressed. The production of the book is excellent and the writing clear and interesting.

***Simulium* and Onchocerciasis in the Northern Territories of the Gold Coast.** By G. Crisp. 1957. Pp. 171, 51 figs., 37 tab., bibl. Lewis, London. 57*s.* 6*d.*

This exhaustive report of the work carried out by the Entomological Unit in the recent survey of Ghana, sponsored by the British Empire Society for the Blind, makes interesting and most informative reading. In the region covered there are one million Africans and it is estimated that half of this number have onchocerciasis, 30,000 of them suffering resultant blindness. Whole villages have been depopulated by the scourge of *Simulium* and as the inhabitants travel further south they spread the infection.

The author has organized his report well and the reader is taken through every stage of the life of *Simulium*, with full descriptive detail of its habitat, predilections, and incidence. The careful work of the exploratory research team is reflected in the wealth of tabulated detail, and after digesting this no one can fail to appreciate the real menace of *Simulium* if allowed to carry out its life cycle without countermeasures being taken.

The author is not content merely to explain the results of his survey. He goes further to outline plans to combat the fly, plans which again reflect the exactitude of his team's work in pin-pointing foci where *Simulium* may most readily and radically be controlled.

The illustrations are good and the production as a whole redounds to the credit of the sponsors and the Entomological Unit. One now looks forward to the publication of the report of the Ophthalmological Unit.

Corneal Lenses. (La pratique des lentilles cornéennes.) By F. de Lesdain (with preface by L. Guillaumat). 1957. Pp. 118, 28 figs. Masson, Paris. (800 *Fr. frs.*; 16*s.*)

The author is a French ophthalmologist who has had the opportunity of studying the records of 2,000 patients fitted with precorneal lenses. From these records he has selected 300 for the purposes of this book, which discusses the indications and contraindications for the use of these lenses, their manufacture, their fitting, and the conditions necessary to secure satisfactory wearing.

The book contains some unexpected ophthalmology and even stranger optics. Thus: "Latent hypermetropia is usually accompanied by symptoms of irritation of the eye, such as blepharitis, photophobia, excessive watering, etc., all of which are greatly exaggerated by the use of corneal lenses" (p. 21).

"Binocular aphakia is not often seen since ophthalmic surgeons know very well the difficulties to be encountered by the patient in fusing the images after the correction, however perfect, of his two eyes by spectacles, so that one is reduced usually to accepting operation on one eye only and with it sacrificing permanently stereoscopic vision" (p. 22).

". . . a lens with parallel faces therefore of null power" (p. 4).

"The thickness of the lens has no role to play in the optical correction" (p. 51).

Notwithstanding such imperfections the book is a valuable appraisal of the use of corneal lenses as seen by the ophthalmologist.

Medical contraindications to the use of corneal lenses are listed by the author as

follows: hypermetropia, and especially latent hypermetropia; astigmatism exceeding 2·0 D; ectropion; entropion; blepharitis; wide palpebral fissures; all affections of the cornea; severe keratoconus; corneal ulcers; anaesthesia or reduced sensitivity of the cornea. He does not think they should be used for children except in high myopes and perhaps some cases of moderate astigmatism. It is surprising to find listed as contra-indications for corneal lenses those very conditions which, in Great Britain, have come to be regarded as medical indications for full-sized contact lenses, and to find excluded such conditions as hypermetropia and higher degrees of astigmatism. The admitted limitations would seem to rule out corneal lenses unless very real advantages can be demonstrated for those cases to which they are applicable. Micro-lenses, which are considered at length, are even more limited in application.

The author is frank about the dangers of these lenses. He admits that the very many reports of injury and ulceration arising from their use are justified and proposes to deal with the problems by stringent ophthalmological supervision. It is illuminating to read (p. 77) that small erosions of the cornea are frequently caused at the first fitting session and that disinfectant drops should be ordered routinely. It is apparent throughout the book that corneal lenses give a good deal of trouble from heterophoria. The reviewer feels that a great deal of the orthoptic work advocated in this book arises out of the instability of these lenses.

After the fourth session with the ophthalmologist the patient may wear his lenses on his own; the following comments (p. 90) are revealing:

"Only after several months conscientious perseverance is it possible finally to assess the daily tolerance. . . . In the early days there is always a reaction comparable to that of a small foreign body planted on the cornea, characterized clinically by dull pain, pericorneal and conjunctival injection, severe photophobia, a certain amount of watering, and even a mucopurulent secretion. . . . The watering is almost invariably present for quite a long time in the majority of wearers and only disappears slowly. It is a very considerable nuisance if people have any obstruction to the tear passages. Bouts of blepharitis appear commonly, especially in hypermetropes and astigmatic patients in the first few weeks. They respond to treatment satisfactorily. . . . Trouble with binocular vision not present when wearing spectacles, and especially when the two eyes have been brought up to a better visual acuity—headache, malaise, vertigo, vomiting may all be seen. . . . Latent hypermetropia becomes manifest and it can be a nuisance. . . . Glare is frequently complained of, especially in high degrees of myopia. It disappears slowly in the course of several weeks. Glasses can be worn over the contact lenses . . ." [to remedy this].

Finally the author presents an analysis of replies to a questionnaire sent out to 277 people who had had their lenses at least 6 months. The results claimed are good, but we are not told how the people to whom the questionnaire was sent were selected out of the 2,000 dossiers at the author's disposal, nor is there any further follow-up.

The author has approached his problem with sincerity and has not hesitated to record the limited scope and even the very real dangers of corneal contact lenses. That this book could be presented in 1957 on the grounds that these corneal lenses are an advance upon the full-sized contact lenses available in France is astonishing. The reviewer, with experience of some 2,000 cases fitted with full-sized contact lenses under the National Health Service in England, puts aside the book with an acute sense of unreality; it is as though one had happened upon a contemporary Listerian polemic.

Besnier-Boeck-Schaumann Disease. By W. WEGNER and K. WURM, with the collaboration of L. Heilmeyer, J. Könn, E. Schimkat, and A. Stühmer. 1957. *Klin. Mbl. Augenheilk.*, Suppl. 27. Pp. 131, 72 figs (9 col.), 9 tab., bibl. (D.M. 17·60; 30*s.*).

This is an interesting monograph on that pathological puzzle which is generally termed

Boeck's sarcoid, one of those loose groups of lesions characterized by the formation of multiple tumours of a granulomatous type and generally of a benign prognosis. The most common site of the lesion is the skin or subcutaneous tissue, but its occurrence in the uveal tract is well known. In the present monograph a high percentage of cases of chronic iridocyclitis is considered to belong to this category. There are many theories as to the aetiology of this disease—that it is caused by a virus; that it is a non-specific reaction perhaps to some non-organismal agent; and so on—but perhaps the most common theory is that it is a benign form of tuberculosis occurring in the presence of high immunity and low allergic reactivity. The last theory is favoured by the authors, and many observations are quoted bringing it into the same family as erythema nodosum, lichen scrofulosum, and lupus, the varying tissue reactions depending on the relation between the degree of immunity and allergy present in the particular patient. The monograph represents a persuasive and careful clinical study, dealing not only with the dermal and systemic aspects of the disease but also in considerable detail with a large series of 172 cases with ocular complications.

Problems of Vision in Flight at High Altitudes. By THOMAS C. D. WHITESIDE. 1957. Pp. 162, 64 figs., 8 tables, bibl. Published for and on behalf of the Advisory Group for Aeronautical Research and Development North Atlantic Treaty Organisation by Butterworth's Scientific Publications, London. (35*s*.). American edition published by Interscience, New York. ($5).

Squadron-Leader Whiteside has made valuable contributions to the practical problems of vision which face those who fly at high altitudes. His book is based entirely on his own experiments and on his own experiences in flight above cloud.

This is a fascinating book to read, for it is so arranged that it takes the reader through the investigations in the order in which they were carried out. The short summary at the end of each section and the opening paragraph of the next section ensure continuity of thought. The historical survey at the beginning of the book outlines the problems arising from the increased speed of air travel and the physical conditions peculiar to flight in the stratosphere.

The author not only explains the physical causes of such phenomena as haze at high altitudes, empty field myopia, and glare, but also their physiological effects and their relationship to anoxia.

Throughout the book there is a strong practical approach to the problems investigated and there is useful information which will help in the construction of aircraft cockpits and the illumination of instrument panels and the production and proper use of flying visors or goggles.

This book will be of interest to all physiologists and ophthalmologists, but especially to those medical officers who are concerned with the welfare of flying personnel.

The only criticism that the reviewer would like to make is that the constant repetition of facts is somewhat irritating and that the problems discussed might with advantage have been arranged in a more orderly sequence.

The references are excellent and the author has thoroughly reviewed the previous literature on the subject.

Stereoscopic Pictures. (Stereoskopische Bilder.) 1956.

A new set of thirty cards for use in a stereoscope has been published by Johann Ambrosius Barth of Leipzig. This set is a modern version succeeding the old Krolls Charts and the later Sattler's Charts, and should be useful in the treatment of strabismus in young children. Dr. Sachsenweger has designed this new series in black and white, using the strong contrast of silhouettes to give visual stimulus, to correct the habit of suppression, and to develop normal binocular vision.

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NOTES

Ophthalmological Society of the United Kingdom

The 77th Annual Congress of the Ophthalmological Society of the United Kingdom was held at the Royal Society of Medicine, London, on April 11, 12, and 13, 1957, under the Presidency of Mr. J. J. Healy. A record number of members and their guests attended, including the members of the International Council of Ophthalmology which met in London on April 10. A wide variety of interesting papers was read.

Presidential Address

After welcoming members of the Society and the many visitors from Britain and overseas, Mr. Healy delivered his presidential address entitled:

The Intra-Ocular Circulation in Arterio-Sclerosis and High Blood Pressure

He gave a comprehensive picture of arterio-sclerosis and particularly of essential hypertension, necessary for the interpretation of the fundus picture in these diseases. He discussed the aetiological and pathogenic theories of hypertension, which are largely based on the evidence of experimentally produced and secondary hypertension, and noted that although physio-pathological research had made some progress, no definite results had yet emerged. He pointed out that arterio-sclerosis might be present as a senile regression in the retinal and choroidal vessels, and essential hypertension might supervene or arise as a separate entity.

He analysed the changes observed in 200 out-patient fundi and assessed these with special reference to angiospasm, arteriolo-sclerosis, and arteriolo-necrosis. He ended his address with a plea for greater liaison between physician, ophthalmologist, and pathologist.

Bowman Lecture

The outstanding feature of this year's Congress was the 35th Bowman Lecture, given by Sir Stewart Duke-Elder on:

The Aetiology of Simple Glaucoma

Sir Stewart introduced his subject with a discussion of the mechanism of the formation of the aqueous humour in the light of recent biochemical and pathological research, with particular reference to the extensive work carried out under his direction at the Institute of Ophthalmology. He went on to discuss the variations in intra-ocular pressure produced especially by peripheral and central nervous stimulation, and indicated the factors responsible for the instability and range in variation of the intra-ocular pressure characteristic of the glaucomatous eye. He traced the development of the initial functional and consequent organic changes, with their terminal ischaemic effects upon the structures of the anterior and posterior segments of the eye and the optic nerve, and examined their respective roles in the development of clinical simple glaucoma.

Sir Stewart emphasized that glaucoma must not be regarded purely as an ocular disease, but rather as a local manifestation of a more general disorder. Advances in the scientific aspects of the problem have not been accompanied by similar advances in either medical or surgical treatment, which have, in fact, made little progress during the past 20 years.

At the conclusion of his lecture Sir Stewart was presented by the President with the Bowman Medal awarded by the Society.

Symposium on Congenital Cataract

This was introduced by Mr. J. H. Doggart, who stated that, although some slight opacity was visible in a great majority of human lenses, even among the new-born, most

of these partial cataracts were harmless and stationary. Nevertheless, they could not be dismissed as insignificant because (*a*) they might be misinterpreted, and (*b*) they supplied clues for embryological investigation. Differentiation of the various congenital cataracts from other kinds of lens opacity was impossible without careful study of the living lens.

Mr. Doggart then briefly surveyed benign, congenital, and hereditary cataract, and drew attention to those opacities which do interfere with function because of their size or situation, or because of additional lenticular defects. He made special mention of rubella and its implications, and finally considered some types of hereditary cataract.

Mr. A. B. Nutt, after a brief review of the literature on the surgical aspects of the subject, emphasized that the results of surgery for congenital cataract were disappointing and that the prognosis must therefore be guarded. Having classified the cases requiring surgical treatment, he gave a brief résumé of the operations commonly used and of their complications and the methods adopted to avoid them. He thought that the poor functional results were in many cases due to associated congenital anomalies.

Ocular Aspects of Diabetes

This was the principal subject for discussion at the Congress. The discussion was opened by Prof. G. I. Scott, who described the problem of diabetic retinopathy and the inconclusive evidence that still rendered its aetiology so obscure.

Prof. Scott confirmed that the retinopathy occurs in the absence of the generalized hypertension of arteriosclerosis or of a local retinal arteriosclerosis, and that the development of retinopathy depended primarily on the duration of the diabetes and not on its severity. He also drew attention to the two different types of retinitis proliferans that are characteristic features in its later stage: the typical product of vitreous haemorrhage, and the gradual development of vascular loops which so often resulted in a *rete mirabile*. We knew that the tendency to diabetes could be inherited, but there seemed to be no genetic stigma that predisposed to the retinopathy, and Prof. Scott quoted a case of his in which retinopathy occurred in diabetes following a pancreatic lesion. He also quoted an interesting family who regularly developed an optic atrophy in association with their diabetes, but not a retinopathy. Retinopathy did not seem to be attributable to capillary fragility, but was always accompanied by a disturbance to carbohydrate metabolism of the diabetic type. He was in the process of investigating whether diabetes was commoner in the well-controlled type and whether it had any altered frequency in those with a high renal threshold.

Dr. Norman Ashton then discussed the relationship between diabetic retinopathy and glomerulosclerosis as seen in man and in experimental animals. In a *post-mortem* series of 203 diabetic cases, he had found retinopathy present in 67·4 per cent. and glomerulosclerosis in 36·9 per cent. The main conclusions drawn from the study of this material were:

(*a*) that retinopathy preceded glomerulosclerosis, and in its early stages might exist without the renal lesion,
(*b*) that diabetic glomerulosclerosis on the other hand was always associated with retinopathy,
(*c*) that although practically all stages of the two lesions could co-exist, severe retinopathy was almost always associated with glomerulosclerosis, and the proportion of cases with severe glomerulosclerosis increased with the severity of the retinopathy.

The close relationship between the incidence of the two lesions and their histological similarity suggested a common cause, but there were several points which were difficult to explain, and the relationship between the two lesions might not in fact be as close as previously supposed.

On the experimental side, no worker had yet succeeded in reproducing a retinopathy which could be accepted as analogous to that seen in human diabetes, apart from isolated components of retinopathy produced by a variety of experimental procedures; lesions resembling diabetic glomerulosclerosis had, however, been repeatedly demonstrated experimentally. There was considerable evidence to show that these lesions might be attributable to lipaemia, for cortisone was known to induce lipaemia in rabbits, and the lesions could be prevented by the simultaneous administration of heparin, and reproduced by other forms of experimental hyperlipaemia. It had been shown that fat emboli alone were insufficient to produce characteristic retinal and renal lesions, but in man it seemed possible that a complex macro-molecular substance consisting of

fat, protein, and mucopolysaccharide, by impeding or obstructing the capillary circulation or by forming intramural deposits, could give rise to the various manifestations of diabetic micro-angiopathy. The evidence that hyperadrenal activity was of significant importance in the process was at present contradictory.

The constant association between diabetic glomerulosclerosis and retinopathy in human diabetes had not been paralleled in any experimental work, so that they were still in doubt whether the experimental renal lesion was in fact analogous to that seen in man. If it was eventually proved to be so it would then be necessary to modify the present concept and to consider that diabetic retinopathy, at least in its early stages, might have a different histogenesis and should be treated as a separate experimental problem.

Finally, Dr. J. D. N. Navarro gave a general assessment of the picture from the physician's point of view, discussing the incidence of diabetic retinopathy and its possible relation to a relative increase in adrenal cortical activity. After reviewing the two groups, insulin-deficient and insulin-resistant, he concluded that the clinical evidence pointed to "prolonged sustained hyperglycaemia, or something closely related to it, as the cause of the retinitis". Discussing the management of the insulin-resistant group, he felt that the principal concern should be to control their obesity. The danger of carbutamide in promoting the risk of retinal damage was mentioned. He had subsequently tried tolbutamide, which was slightly different chemically and not a true sulphonamide; the results had been satisfactory with negligible side-effects, but prolonged trial would be necessary with these new drugs before they could be recommended for widespead use, and even then they would only be suitable for a small proportion of cases. More radical measures included hypophysectomy, which had a considerable mortality and the effects of which although generally favourable were difficult to assess.

Communications

Intravitreal Vitreous Injection in Retinal Detachment Surgery.—The role of this procedure in retinal detachment surgery was discussed by Mr. P. McG. Moffatt and Mr. C. Dee Shapland.

Mr. Moffatt outlined the historical background, and discussed the changes occurring in the vitreous in cases of retinal detachment and the rationale of vitreous replacement as a method of treatment.

Mr. Dee Shapland described the technique for obtaining the donor vitreous and its subsequent injection under pressure into the recipient eye. He then analysed the results obtained in a small series of his own cases and in those of Mr. Moffatt. He discussed the indication for the procedure in cases of retinal detachment in the light of the present procedure.

Sclera in Retinal Detachment Surgery.—Mr. George Black discussed the anatomical and physiological considerations and criticized present-day techniques in regard to their effect upon the sclera, such as local necrosis, injury to nerves and blood vessels, and effects upon anterior structures. He noted the variable effects of diathermy treatment when mediated through the full thickness of the sclera, and described his own method of scleral trap-door access to the choroid and its application.

Ptosis Operation.—Mr. H. B. Stallard advocated the anterior surgical approach to the levator palpebrae superioris which exposed it in its normal relationship to other structures, revealed any unusual attachment of this muscle to the orbital fascia, allowed the separation of any fascial connexion with the superior oblique tendon sheath, and permitted a greater length of the muscle to be resected and more accurate suturing of the resected muscle to the tarsal plate than by other methods of exposure. He described a new lid guard for use in this operation and illustrated the technique with a coloured ciné film.

Lamellar Keratoplasty.—Prof. A. Franceschetti showed a film demonstrating a new instrument for cutting lamellar corneal grafts. Its application in lamellar keratoplasty were described and illustrated by a ciné film.

Toxoplasmic Uveitis.—Mr. E. S. Perkins discussed the probable incidence of infection in over 250 cases of uveitis together with the related laboratory findings. Treatment with Daraprim had given excellent short term results in some cases.

Lacrimal Obstruction.—Mr. F. W. Law showed the *x*-ray apparatus in a case of lacrimal obstruction of unusual clinical behaviour, and gave details of the technique of this method of examination, using Neohydriol as a contrast medium.

Marcus Gunn Syndrome.—Mr. Rupert Parry gave a pictorial demonstration of an unusual case of this syndrome.

Ocular Changes after Rupture of the Liver.—Mr. G. T. Willoughby Cashell described a case in which retinal changes appeared in both eyes after a traumatic rupture of the liver, and briefly discussed the ocular effects of remote injuries.

Phacolytic Glaucoma.—Dr. P. Schofield gave an account of the association of glaucoma with hypermature cataract. Although recognized since 1900, this had only recently been defined as a clear-cut pathological entity and named "phacolytic glaucoma". Basing his paper on the histological examination of three cases, Dr. Schofield described the pathology and pathogenesis of the condition. He presented for discussion some features of possible diagnostic and therapeutic importance.

Venous Obstruction at the Disc in Chronic Glaucoma.—Mr. J. H. Dobree described macroscopic lesions occurring on glaucomatous optic discs, including central vein thrombosis, venous coils, anastomotic vessels, and haemorrhages at the disc margin. These lesions had been observed in an investigation of a series of 200 eyes in consecutive cases, a view of the cases having to be omitted as no ophthalmoscopic view of the optic discs was obtainable. He discussed the relationship of these vascular changes to other signs of glaucoma, such as the prevailing level of tension, cupping, atrophy, and field defects. In a controlled series without tension but with gross arteriosclerotic vessel changes, quite different disc appearances were observed. He thought that the main factor determining the onset of the venous lesions was probably the glaucomatous cupping. He discussed the possible mechanisms which played a part in their formation, and their significance with regard to prognosis.

Foreign Body Detector and Locator.—Mr. M. J. Roper-Hall described a new electronic instrument by which small metallic particles, both magnetic and non-magnetic, could be detected and an assessment made of their chemical and physical properties. Two sizes of probe had been made, $\frac{1}{4}''$ and $\frac{1}{2}''$ thick, the latter being sensitive to very small metallic fragments at a distance of 15 mm. The prototype instrument had already been used for confirming the presence of intraocular foreign bodies originally detected by *x*-ray examination and localization, and had also been used to distinguish magnetic and non-magnetic metallic fragments seen by *x*-ray. The instrument was insensitive to other metal bodies (such as dental fillings and the operating table) at distances greater than 3 cm. The sensitivity of the probes increased with their size and although they were able to detect smaller metallic fragments, the range up to which other metal bodies affected them was greater. The $\frac{1}{4}''$ probe was unaffected by metal bodies at a distance greater than 4·5 cm.

Mr. Roper-Hall said that the instrument was still being developed and that its uses were being extended from ocular to general surgery. He described in detail three cases in which it had been successfully used.

Case of Retinoblastoma with post-mortem *Findings.*—Mr. John Ellison described the case of a small child who had a retinoblastoma with extension into the optic nerve. A second operation was undertaken to remove the optic nerve remaining in the orbit and the pathological report on this indicated that the removal had been clear of growth. Specimens of the eye, skull, brain, and liver were shown, indicating the extent of the metastases from which the child subsequently died some 6 months later.

Clinical and Pictorial Survey of Uveitis in Childhood.—Mr. Joseph Minton gave an account of three children suffering from severe uveitis, in one of whom the full clinical picture of Still's disease developed some time after the original uveitis. He pointed out the value of treatment with cortisone and ACTH, and more particularly with the new derivatives, prednisone and prednisolone. One of the cases which had responded indifferently to treatment with cortisone was markedly improved by prednisolone. The clinical features of the three cases were shown by coloured lantern slides.

Pathogenesis of Ocular Onchocerciasis.—Dr. F. C. Rodger described an extensive field survey and both clinical and experimental work undertaken to determine the types of case infested with onchocerciasis in which ocular lesions were most likely to be found. To estimate the density of infection he had prepared an index which related the degree of infestation and its anatomical distribution over the body with the likelihood of developing ocular onchocerciasis. He had found cases in which maximum infectivity was present by his standard of examination, including actual invasion of the eyes, without the development of ocular lesions. This he attributed to an immunity developed by the individual as a result of the infestation in other parts of the body.

Experimental work with animals had shown conclusively that it was the dead parasite which led to an inflammatory reaction, and nearly all the manifestations of human onchocerciasis had been reproduced in the rabbit.

Dr. Rodger found a low individual density figure in some cases with posterior segment lesions, particularly choroido-retinal degeneration, and postulated that the damage to the tissues might be due to a toxin secreted by the adult worms. He also discussed the influence of vitamin A deficiency upon the degree of tissue damage.

Pattern of Conjunctivitis at Moorfields during 1956.—Mr. Barrie R. Jones had investigated a proportion of the cases presenting at Moorfields with conjunctivitis during 1956, in order to establish the aetiology of the condition. The particular aim was to evaluate the role of various viruses in the production of conjunctivitis and kerato-conjunctivitis.

He found that a few cases were due to some of the well-recognized bacterial infections, that several cases were associated with infection by adeno-viruses (A.P.C. viruses) and that in others there was evidence of infection by the virus of herpes simplex. Among other infections seen in association with conjunctivitis, he found molluscum contagiosum, vaccinia, influenza, and cat scratch fever.

The seasonal incidence of both the bacterial and the virus types of conjunctivitis was indicated diagrammatically and colour photographs were shown of a number of cases seen during the investigation.

Middlemore Prize

The Middlemore Prize, which consists of a cheque for £50 and a certificate, was founded in 1880 by the late Richard Middlemore, F.R.C.S., of Birmingham, to be awarded for the best essay or work on any subject which the Council of the British Medical Association may from time to time select in any Department of Ophthalmic Medicine or Surgery.

The Council of the British Medical Association is prepared to consider an award of the Prize in the year 1958 to the author of the best essay on:

Local Antibiotic Treatment in External Ocular Disease

Notice of intention to enter for the Competition should be made on the appropriate entry form, copies of which can be obtained from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

Essays must reach the Secretary on or before *January 31, 1958*. Each essay must be unsigned and accompanied by a note bearing the name and address of the author. Previous prizewinners are not precluded from entering. If no essay of sufficient merit is submitted, the prize will not be awarded in 1958, but will be offered again in the following year.

A. Macrae,
Secretary

Nathaniel Bishop Harman Prize for Research in Hospital Practice

The Council of the British Medical Association is prepared to consider the award of the Nathaniel Bishop Harman Prize in the year 1958. The value of the prize is approximately £100.

The purpose of the prize is the promotion of systematic observation and research by consultant and specialist staff and senior registrars of hospitals not attached to recognized medical schools.

It will be awarded for the best report on original clinical research in a form suitable for publication. The work submitted must include personal observations and experiences collected by the candidate in the course of his practice. A high order of excellence will be required. No report or study that has previously been published in the medical press or elsewhere will be considered eligible for the prize.

Any registered medical practitioner on the staff of a hospital in Great Britain or Northern Ireland, who is not a member of the staff or a recognized undergraduate or postgraduate medical school, is eligible to compete.

If any question arises in reference to the eligibility of a candidate or the admissibility of his entry, the decision of the Council shall be final.

Should the Council of the Association decide that no entry submitted is of sufficient merit, the prize will not be awarded in 1958, but will be offered again the year next following this decision, and in this event the money value of the prize on the occasion in question shall be such proportion of the accumulated income as the Council shall determine.

Each entry, which must be typewritten or printed in the English language, should be unsigned, but accompanied by a note bearing the name and address of the author. It is suggested that reports should consist of from 3,000 to 10,000 words.

Candidates are required to complete an entry form, a copy of which can be obtained from the Secretary. Reports and entry forms must reach the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than *January 31, 1958*.

Inquiries relative to the prize should be addressed to the Secretary.

A. MACRAE,
Secretary

FACULTY OF OPHTHALMOLOGISTS

At a meeting of the Council of the Faculty of Ophthalmologists in May, 1957, the following Officers were elected for the year 1957–58:

President: Mr. L. H. Savin
Vice-presidents: Mr. E. G. Mackie and Prof. G. I. Scott
Hon. Secretary: Mr. E. F. King (re-elected)
Hon. Treasurer: Mr. A. McKie Reid (re-elected)

APPEAL FOR BOOKS AND EQUIPMENT

"Our Eye Department is in a pitiable condition for want of books and journals, transactions, reprints of articles on diseases of the eye, and also good surgical and diagnostic equipment. I request you to kindly help us in all possible ways by passing on my request to the members of your Society so that they may do their part."

The Honorary Medical Superintendent,
St. George's Mission Hospital, Punalur P.O., Travancore, S. India.

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OBITUARY

James Fison

It is with deep regret that we learn of the death, on April 20, 1957, of Dr. James Fison, at the age of 74; his health had been failing for some months. Educated at Sidney Sussex, Cambridge, he proceeded to St. Bartholomew's Hospital. He filled postgraduate appointments, at St. Bartholomew's and Moorfields, but his career was interrupted by a period of treatment for phthisis in a sanatorium in Switzerland. In spite of this handicap, however, he joined the Royal Navy in the first World War. Thereafter, he settled in practice in Harrogate. Here he acted as ophthalmic surgeon to the Harrogate General Hospital, and the Ripon and District Hospital, and was consulting ophthalmic surgeon to the Leeds Public Dispensary and Hospital.

For his skill, knowledge, and sanity of outlook, he will be greatly missed by his colleagues, and he will be remembered with gratitude by a host of patients for his meticulous care and kindliness.

Fison was a strikingly handsome man of great charm and a fine presence; he seemed to be made of a more highly-refined metal than most of us. He was possessed of a delicate wit and took delight in all beautiful things. He was a horticulturist of no mean order, and a musician of ability; a vinery and an organ were part of the trappings of his home; at one time he was addicted to golf, at which his style—of which he professed to be inordinately proud—was more entertaining than effective: he was indeed a charming companion.

He leaves a widow, and three sons who have followed him to St. Bartholomew's, one of whom is well established in London in his father's specialty: to them we extend our deep sympathy.

Alfred Clarence Norman, C.B.E.

Dr. A. C. Norman, formerly Professor of Radiology in the Royal College of Baghdad, died at his home in Essex on April 23, 1957, at the age of 75. Although he ceased to practise ophthalmology when he was commissioned in the R.A.M.C. in 1914, it is of interest to recall that he was the first to use a silver limbal ring (about 1914) for *x*-ray localization of intra-ocular foreign bodies.